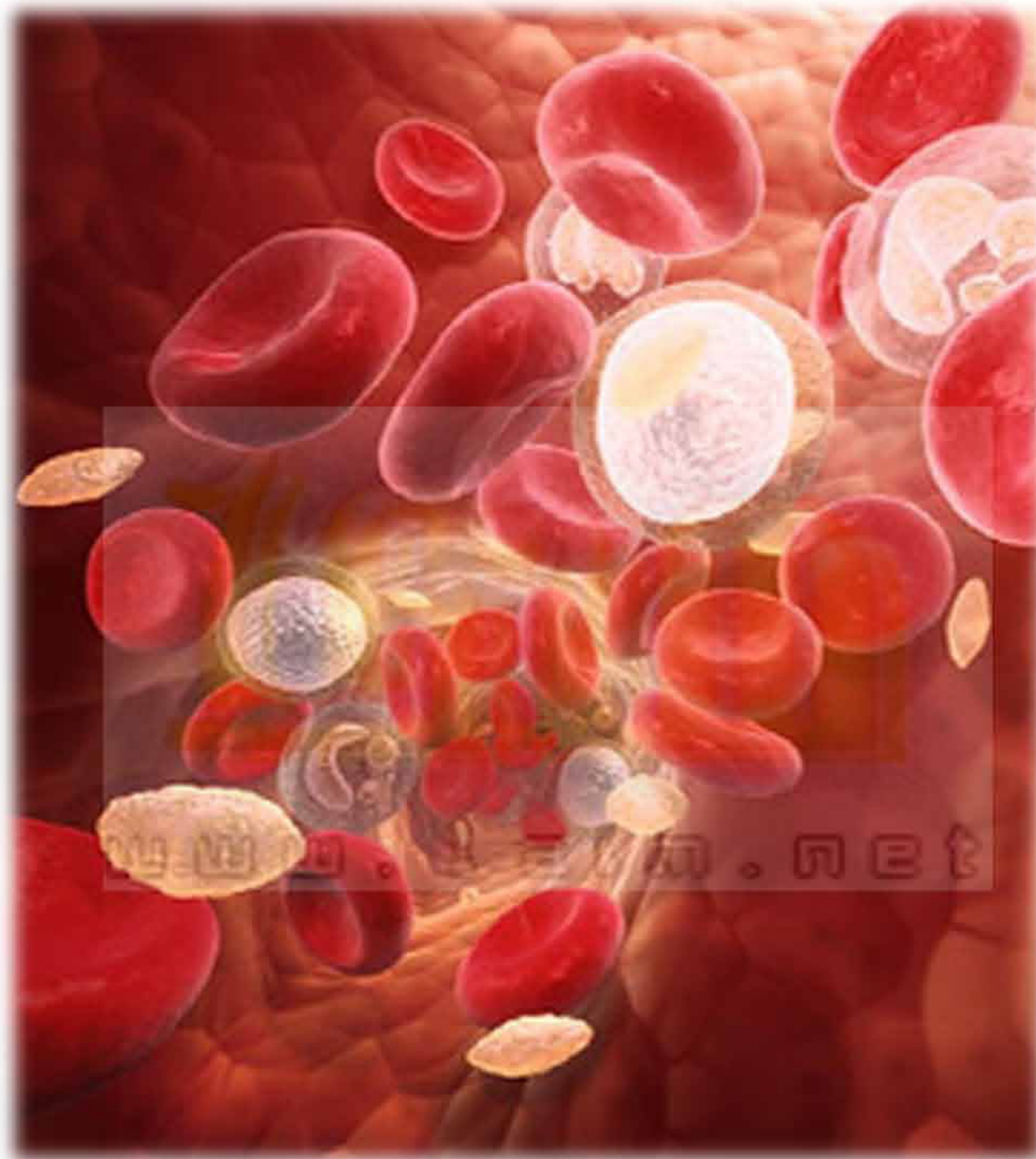


BLOOD



2 0 0 9 - 2 0 1 0

Index:

LEUCOCYTES:

- **LEUKEMIA.**
- **LYMPHOMA.**
- **MYELO-PROLIFERATIVE DISORDERS.**
- **GAMMOPATHIES.**
- **WBCs COMPARISON.**

RBCs: ANEMIA + OTHERS.

BLEEDING DISORDERS:

- **PURPURA.**
- **CO-AGULOPATHIES.**

VISIT...

LANZAROTE
Caliente.COM

LEUKEMIA

ACUTE

CHRONIC

LYMPHO-BLASTIC

MYELOID

MYELOID (M)

LYMPHO-CYTIC

لوكريميا الأطفال .. تستجيب للعلاج

لوكريميا الشباب ... عنيفة جدا

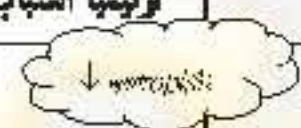
لوكريميا منتصف العمر

لوكريميا العواجز ... شبيهة الـ Lymphoma

Malignant proliferation of

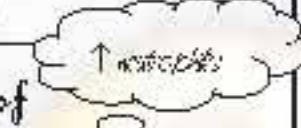
B/M Blast Cells $\Rightarrow$ B/M & Tissue infiltration.

(ALL = 75% B CELL / 25% T CELL WHICH IS RESISTANT TO TTT. $\Rightarrow$ WORSE PROGNOSIS)



Malignant proliferation of

Myelo Promyelocytes & Mature Neutrophils.
(SMALL CELLS..... ESCAPED B/M.... TISSUE INFILT. + LATE B/M FAILURE)



Accumulation of

Mature B lymphocytes in Blood, BM, Lymphoid T.
"CELL OF ORIGIN B-LYMPHOCYTE..... ABNORMAL ICB"

> CL/P

1) BM INFILTRATION $\Rightarrow$ BM FAILURE

- $\downarrow$ RBCs $\rightarrow$ ANEMIA $\rightarrow$ PALLOR.
- $\downarrow$ WBCs $\rightarrow$ INFECTIONS $\rightarrow$ FEVER.
(SOME THREAT DOESN'T RESPONDING TO TTT. / PER-ANAL ANALYSIS)
- $\downarrow$ PLATELETS $\rightarrow$ BLEEDING. (EPSTAXIS / PURPURA)

2) TISSUE INFILTRATION:

- BONE $\Rightarrow$ fractures / sternal tenderness.
- LIVER - SPLEEN - LN++ ... (ALL > AML)
- CNS $\Rightarrow$ MENINGEAL INFILT.
- RETINA $\Rightarrow$ $\downarrow$ VISION.
- HEART $\Rightarrow$ CARDIOMYOPATHY.
- LUNG $\Rightarrow$ HEMOPTYSIS.
- PORTA HEPATIS $\Rightarrow$ OBST. JAUNDICE.
- KIDNEY $\Rightarrow$ TUBULAR DAMAGE $\Rightarrow$ $\downarrow$ K $\downarrow$ NA.
- SKIN $\Rightarrow$ ITCHING. "LEUKEMIA CUTIS"
- LEUCO-STASIS.

1) ASYMPTOMATIC. (30%) ACCIDENTLY DISCOVERED.

2) MASSIVE SPLEEN $\Rightarrow$ PAIN

- DRAGGING PAIN IN LT. HYPO-CH.
- STITCHING PAIN DT SPLENIC INFARCTION. DT LEUCOSTASIS.

3) BONY ACHES + BLOOD CELLS

- $\downarrow$ RBCs $\Rightarrow$ ANEMIA.
- N. NEUTROPHIL $\rightarrow$ NO INFECTION.
- N. PLATELETS $\rightarrow$ NO BLEEDING.

4) FEVER & SWEATING, (NOT DUE TO INFECTION) ($\uparrow$ WBCs turnover $\rightarrow$ $\uparrow$ BMR $\rightarrow$ low grade fever)

5) LEUCO-STASIS $\Rightarrow$ brain, lung, penis.

6) BLAST CRISIS: "هيقب فتاك هي المشكلة ... هيموت"

(CML TRANSFORMS TO AML $\Rightarrow$ BM failure $\Rightarrow$ DEATH)

1) ASYMPTOMATIC. (mainly)

2) LIVER - SPLEEN - LN++

3) IMMUNE DISORDERS

- $\downarrow$ RBCs $\rightarrow$ AIHA (+ve Coombs' test)
- $\downarrow$ PLATELETS $\rightarrow$ BLEEDING.
- $\downarrow$ IG $\rightarrow$ INFECTIONS E MRSA
أهم حاجة ... هيموت

HUGE SPLEEN (crossing umbilicus)

- CML
- Myelo-fibrosis.
- Amyloidosis.
- CHRONIC MALARIA, "tropical splen"

ACUTE LEUKEMIA

INVEST.

LYMPHO-BLASTIC

MYELOID

• WBCs .. TLC

WHEN TO SUSPECT ALEUKEMIC LEUKEMIA?!

- Infections ... sore throat.
- ↓ Neutrophils / RBCs / platelets.
- BM exam ... Blasts in BM.

VARIABLE SO DON'T DEPEND ON ↑ TLC
BUT excessive BLASTS IN BLOOD IF NOT, SEE BM DT

	SUB-LEUKEMIC LEUKEMIA	ALUKEMIC LEUKEMIA
TLC	NORMAL	NORMAL
BLASTS IN BL.	↑↑	 but BLASTS IN BM.

NORMO / NORMO



• RBCs

• PLATELETS

BM EXAM. "CONFIRMATORY"

- 1) > 20% BLASTS IN BM to exclude ITP in Aleukemic Leukemia
- 2) AML → AUER RODS IN CYTOPLASM OF BLASTS.
- 3) AML → +ve Myeloperoxidase/ (-ve) in ALL

Others

- 1) ↑↑↑ ESR (LEUKEMIA / LYMPHOMA / MM)
- 2) ↑ URIC ACID & LDH DT TUMOR LYSIS \$.
- 3) ↓ ALP. (Variable)
- 4) OTHERS:
 - ✓ KIDNEY & LIVER PROFILE
 - ✓ CT BRAIN
 - ✓ PELVI - ABDOMINAL SONAR.

prognosis

ALL BETTER THAN AML

- 1) AGE: 2 - 10 ys. TLC > 1000,000
- 2) PLATELETS < 25,000 L₃.

CHRONIC LEUKEMIA

MYELOID (M)

Not Viral

LYMPHO-CYTIC

خرافی > 25,000 ⇒ UP TO MILLION / MM³

- MYELO & PRO-MYELOCYTES.
- MATURE NEUTROPHILS. (marked shift to the Lt.)
- BASOPHILIA.
- EOSINOPHILIA.

IN BLAST CRISIS

↑↑ MYELO-BLASTS > 20-30%



NORMAL OR ↑ (MYELO-PROLIF.) OR ↓.

- MYELO & PRO-MYELOCYTES.

- 1) ↓ ALP (dt Immature Malignant WBCs / ↑ in leukemoid reaction)
- 2) ↑↑↑ URIC ACID DT ↑↑ TLC - LDH.
- 3) ↑ VIT. B₁₂ (TUMOR MARKER) DT ↑ WBCS PRODUCTION OF TRANS-COBALMIN I
- 4) PHILADELPHIA CHROMOSOME BY PCR.
 (fusion of Ch. 9 - 22 → Fusion Oncogene
 → Stem cells turn-off apoptosis → ↑ no. in BM & bl.)

BLAST CRISIS.

SUSTAINED ABSOLUTE LYMPHOCYTOSIS

> 5,000 UPTO MILLION / MM³

- DT INFECTIONS
- MATURE LYMPHOCYTES.



(DT BM FAILURE / AIHA)



(DT BM FAILURE / IMMUNE D.)

- IMMATURE LYMPHOCYTES > 30%

- +ve COOMB'S TEST ⇒ AIHA. "WARM AB"
- ↓ Ig OR NORMAL.

REICHTER'S TRANSf (HIGH GRADE LYMPHOMA.

Treatment of Leukemia

Treatment of Leukemia			
ACUTE LYMPHOBLASTIC	ACUTE MYELOID	CHRONIC MYELOID	CHRONIC LYMPHOCYTIC
GENERAL MEASURES: ⇒ نعيش العيان 1) BM FAILURE: a) ↓RBCs ⇒ BL. TRANSFUSION. b) ↓WBCs ⇒ ISOLATION & Abs / Anti-Viral / Fungal Sumin for PNEUMOCYSTIS CARNI. c) ↓PLATELET ⇒ PLATELET TRANSFUSION. (TO > 20,000) 2) LEUKO-STASIS ⇒ Leukophoresis. 3) TUMOR lysis S: ⇒ S. CREATININE a) hyper-Uricemia → ARF (↑ S. Creatinine) ⇒ Allo-purinol + Alkaline DIURESIS. b) hyper-Phosphatemia ⇒ phosphate binders (Ca ₂ CO ₃)		Aim of CML TTT: 1) ↓ TLC ↓ LEUCO-STASIS. 2) Delay BM failure. 3) Control Blas crisis. GENERAL MEASURES.	INDICATIONS of TTT. In CLL: • ANEMIA. (AIHA) • SPLEEN & LN ++++++ • REICHTER'S TRANSFORMATION.
Specific ttt. of BM		Specific ttt.	Stage A: (no BM failure) • NOSPECIFIC TTT. • RE-ASSURE & FOLLOW UP. Stage B: CLL • CHLORAMBUCL + CYCLOPHOSPHAMIDE. • RADIO-THERAPY TO LN.
A) Induction ⇒ (VAP-L) 4 wks الضربة القاضية 1) VINCISTINE 2) ADMARIN. 3) PREDNISOLONE. "LYMPHOLYTIC" 4) L-ASPARAGINASE AIM: DESTROY TUMOR BULK IN BM DESTROY ALL BM (Plate & Normal)	A) Induction: CTA هذا هو لطم 1) 6-MERCAPTOPURINE 2) 6-THIOGUANINE 3) ADMARIN. Destroy ALL BM (Plate & Normal)	1) hydroxy-UREA: ⇒ Myelo-suppressive ⇒ to keep TLC with it Normal ⇒ to avoid leu-stasis 2) INTERFERON: (Anti-prolit.) ↓ PH (+VE) CELLS → ↓ PH CHROMOSOME 3) IMATINIB to CML & BLAST CRISIS. ⇒ (-) TYROSIN KINASE ⇒ ↓ ACTIVITY OF FUSION PROTEINS 4) BLAST CRISIS as ALL / AML. 5) SPLEEN ⇒ Radio-th. / splenectomy. 6) LEUCO-PHARESIS. (DT MILLION TLC) 7) BM TRANSPLANT. "OF CHOICE"	Stage C: 3C 1) CHLORAMBUCL + CYCLOPHOSPH. 2) CORTICO-STEROIDS (IF BM failure + AIHA) 3) ↓RBCs ⇒ PACKED RBCs TRANS. 4) ↓PLATELET ⇒ PLATELET TRANS. 5) RITUXIMAB (MCA AGAINST TUMOR CELLS & CD-20 SA) ➤ SPLENECTOMY if: • AIHA. • HUGE spleen. • Hyper-splenism.
B) Consolidation ⇒ (CC) 4 wks ضمان يسلم و يعيش ثاني 1) 6-MERCAPTOPURINE 2) 6-THIOGUANINE. (AA-C) CNS prophylaxis ⇒ Intrathecal Methotrexate SIGNS OF REMISSION: • improv. CL/P. • BM blasts < 5% • No blasts in bl.	C) Consolidation: (AS ABOVE + CNS PROPHYLAXIS) FOR M, M5		
D) MAINTENANCE ⇒ (MM) 2ys. 1) 6-MERCAPTOPURINE 2) METHOTREXATE	E) MAINTENANCE (MM) صعب جدا اذن الهدف Induction then BM TRANSPLANT.		

FAB classif. Of ALL

- L₁ Small cells.
- L₂ Large cells.
- L₃ Burkitt like large cells.
(VACUOLATED CYTOPLASM V. AGGRESSIVE)

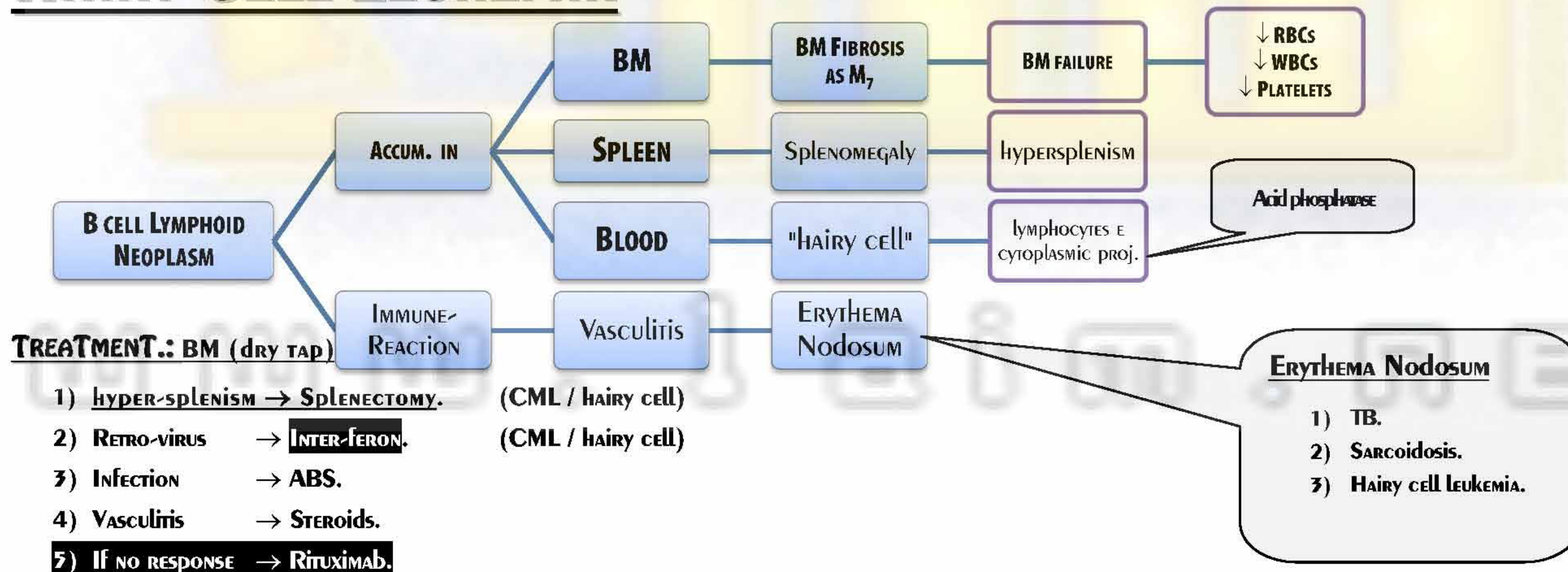
FAB classif. Of AML

M ₀	UN-diff.
M ₁	Myelo-blast + <u>No</u> MATURATION
M ₂	Myelo-blasts + MATURATION.
M ₃	PRO-myelocyte ⇒ DIC
M ₄	Myelo-monocytic.
M ₅	Mono-cytic ⇒ Cum hypertrophy.
M ₆	Erythro-leukemia ⇒ Multi-N. RBC blasts in BM.
M ₇	MEGakaryo-blastic ⇒ v. AGGRESSIVE. "Myelo-fibrosis"

STAGING of CLL

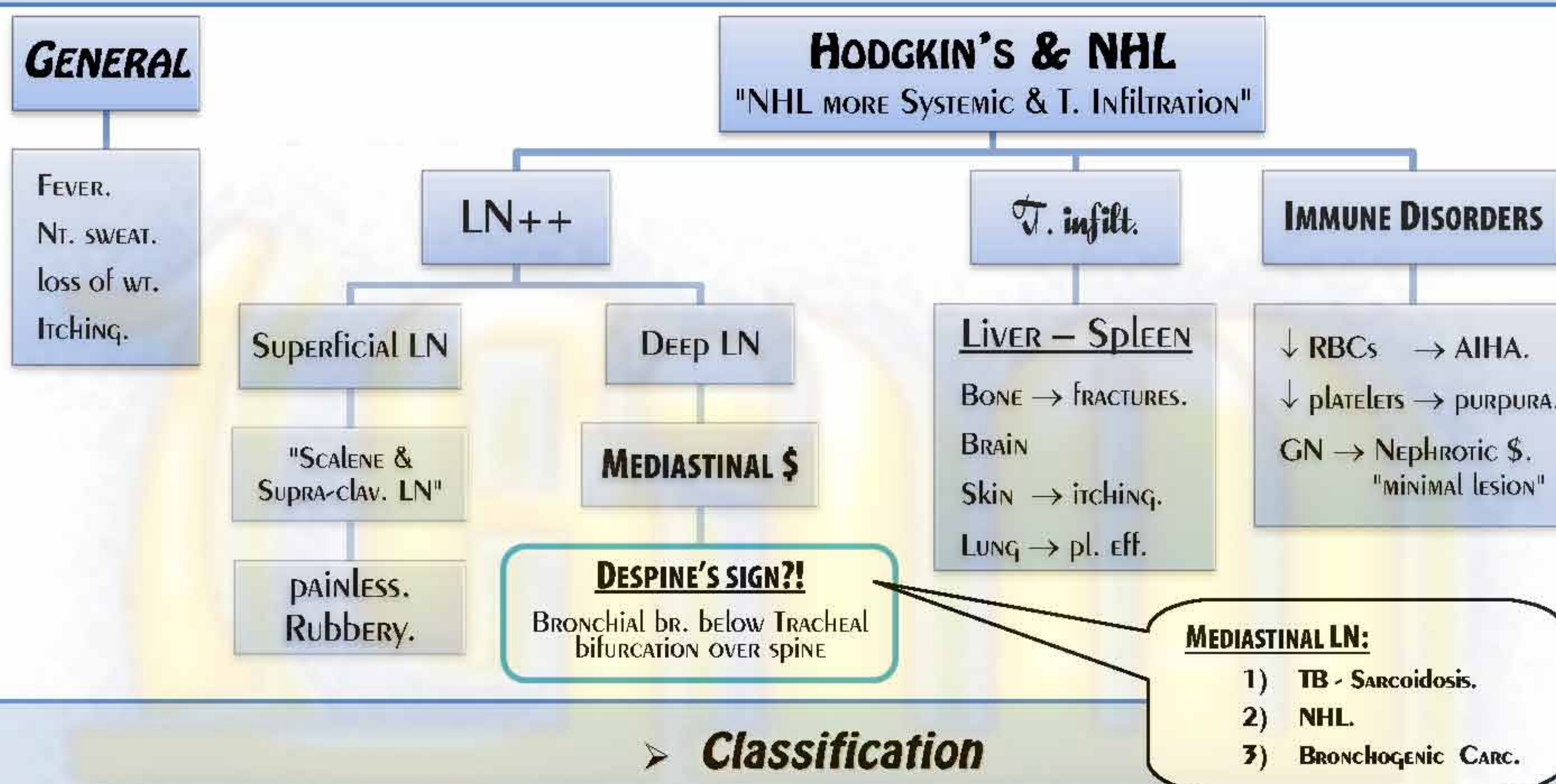
	A	B	C
lympho-cytosis	✓	✓	✓
LN++	< 3 LN++	> 3 LN++	REGARDLESS No.
BM FAILURE	x	x	✓

HAIRY CELL LEUKEMIA



	HODGKIN'S	Non-HODGKIN'S
DEF.	<u>malignant prolif. of Unknown cell</u> (Reed Sternberg Cell)	<u>malignant prolif. of lymphoid cells.</u> (B-cell > T-cell)
Age	1 st peak: (20-30) 2 nd peak: (50-70)	60-75 ys.
etiology	UNKNOWN, NO RELATION TO EBV	1) EBV ⇒ Burkitt's lymphoma. 2) h. pylori ⇒ MALT lymphoma. 3) IMMUNO-comp. ⇒ HIV + post-TRANSPLANT.

➤ **CL/P** (pallor - purpura - HSM)



- **STAGE I** ⇒ SINGLE LN REGION.
- **STAGE II** ⇒ 2 OR MORE LN ON ONE SIDE.
- **STAGE III** ⇒ LNS ON BOTH SIDES.
- **STAGE IV** ⇒ **DIFFUSE EXTRA-LYMPH. (LIVER & BM)**

- 1) **LOW GRADE.**
- 2) **INTERMEDIATE.**
- 3) **HIGH GRADE. "BURKITT & NON-BUTKIT"**

INVEST.

- 1) **CBC:** ANEMIA – **EOSINOPHILIA** - NEUTROPHILIA.
- 2) **↑↑ ESR** **LYMPHOPENIA**
- 3) **↑ URIC ACID & CA⁺⁺.**
- 4) **LN BIOPSY - CXR – CT SCAN. "DIAGNOSTIC"**

- 1) **IG PROFILE.**
- 2) **↑↑ ESR**
- 3) **↑ URIC ACID & CA⁺⁺.**
- 4) **LN BIOPSY & BM EXAM. "DIAGNOSTIC"**

➤ TREATMENT

- 1) **RADIO-TH.** → Stage 1 & 2 + Serious pr. manifest.
- 2) **CHEMO-TH.** → Stage 3 & 4.

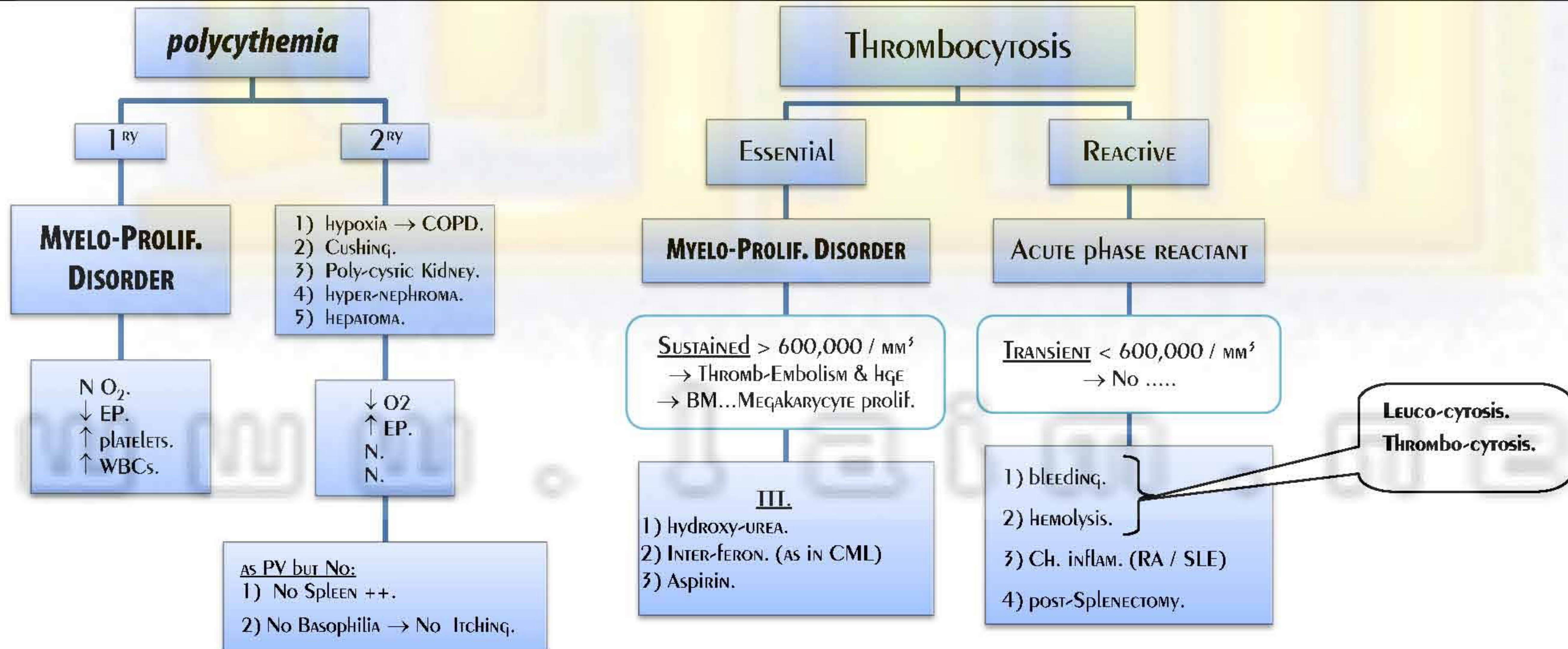
<u>Old</u>	<u>RECENT</u>	<u>MOST RECENT</u>	
<u>MOPP</u>	<u>ABVD</u>	<u>BEA COPP</u>	
• <i>M</i> USTIN.	• <i>A</i> DRIAMYCIN.	• <i>B</i> LEOMYCIN.	• <i>V</i> INCRISTINE.
• <i>V</i> INCRISTINE.	• <i>B</i> LEOMYCIN.	• <i>E</i> TOPOSIDE.	• <i>P</i> REDNISOLONE.
• <i>P</i> REDNISOLONE.	• <i>V</i> INBLASTINE.	• <i>A</i> DRIAMYCIN.	• <i>P</i> ROCARBAZINE.
• <i>P</i> ROCARAZINE.	• <i>D</i> ACARBAZINE.		

- 1) **Low grade NHL:**
 - a) **RADIO-TH.**
 - b) **CHEMO-TH.** → CHLORAMBUCIL – CYCLOPH.
 - c) **RITUXIMAB. "CLL "REICHTER'S TRANSF."**
- 2) **High grade NHL: R-CHOP REGIME:**
 - **RITUXIMAB.** **CYCLOPHOSPHAMIDE.**
 - D XORUBICIN..**
 - V INCITRACIN.**
 - P REDNISOLONE.**

pan-hyper-cellularity of BM • PV → ↑ RBCs MAINLY. • CML → ↑ WBCs. • ET → ↑ PLATELETS • MF → ↑ FIBROBLASTS.		Myelo-proliferative D.	CRITERIA: • Splenomegaly. • Basophilia. • ↑ B₁₂ • Tit. by hydroxyurea	Plasma Cell = GAMMOPATHIES										
poly-cythemia Rubra-Vera		Myelo-fibrosis		MULTIPLE MYELOMA	<i>Walden-strom's</i>									
pan hyper-cellularity of BM mainly RBCs + ↑ WBCs / Platelets ↓ hyper-viscosity \$		pan hyper-cellularity of BM mainly Fibro-blasts ↑↑ MEGA-karyocytes as in M₂ → F-GF → ⊕ FIBROBLASTS IN BM. → BM FIBROSIS. EMH dt BM fibrosis ↓ HSM (Th. Major)		MALIGNANT PROLIF. OF PLASMA CELLS SECRETING MONOCLONAL Ig. (GADE) "old male - bony aches - ↑↑↑ ESR > 100"	MONO-CLONAL D. OF PLASMA CELLS ⇒ ↑↑ IgM secretion (HMW) ⇒ Remains IV. ⇒ Hyper-viscosity \$.									
CL/P														
1) ↑ RBCs ⇒ hyper-viscosity \$: a) PLETHORA. CHF, ↓ CBF "DIZZINESS" b) ENGORGED RETINAL V. → THROMBOSIS. c) VERTIGO - TINNITUS - VISUAL DIST. d) INTERMITTENT CLAUDICATION.		شبه ال CML SO ... BM EXAM. • ↓ RBCs → ANEMIA "EARLY". • ↑ WBCs → LEUCOCYTOSIS REMAINS PERSISTENT FOR LONG TIME. • ↓ platelets → BL. TENDENCY. • HUGE SPLEEN.		MALIGNANT PROLIF. OF BM PLASMA CELLS SECRETES CYTOKINES THAT ⊕ OSTEO-CLASTS BONE RESORPTION HYPER-CALCAEMIA HYPER-URICEMIA "Tumor lysis S" Ig light chain "Toxic to Tubules" Amyloidosis "AL Type" Dehydration RENAL F. BONY ACHES "DT OSTEOLYTIC LESIONS & OSTEOPOROSIS" VERTEBRAL COLLAPSE SC compr. tingling & paraplegia BM INFILT. 1) ↓ RBCs ANEMIA 2) ↓ Platelets → BL. TENDENCY. AS ALL but No HSM & LN++ ↑↑ Ig IMMUNE-disorders INFECTIONS dt defective opsonization of capsulated ORG. "PNEUMOCOCCI" ↑↑ M protein Hyper-viscosity \$		1) Nose bleeds, RETINAL HGE. 2) LIVER - SPLEEN - LN ++ 3) hyper-viscosity \$: • Cong. HF • Vascular occ. c gangrene. • Raynaud's ph. PN. • Cyanosis in fingers. 4) No RENAL DISEASE.								
➤ INVESTIGATIONS														
1) CBC ⇒ ↑↑ all cells mainly RBCs. (↓ ESR) 2) BM EXAM. 3) CRITERIA FOR DIAGNOSIS OF PC VERA. <table><tr><td>A₁ ↑ Red cell mass.</td><td>B₁ ↑ Platelet > 400.000</td></tr><tr><td>A₂ NORMAL O₂ (↓ EP)^{no} exclude hypoxia in 2nd polycyth.</td><td>B₂ ↑ TLC > 12.000</td></tr><tr><td>A₃ Splenomegally</td><td>B₃ ↑ ALP. (WBCs ARE MATURE)</td></tr><tr><td></td><td>B₄ ↑ Vit. B₁₂ (CML & PV)</td></tr></table>		A ₁ ↑ Red cell mass.	B ₁ ↑ Platelet > 400.000	A ₂ NORMAL O₂ (↓ EP) ^{no} exclude hypoxia in 2 nd polycyth.	B ₂ ↑ TLC > 12.000	A ₃ Splenomegally	B ₃ ↑ ALP. (WBCs ARE MATURE)		B ₄ ↑ Vit. B ₁₂ (CML & PV)	1) CBC: a) ↓ RBCs → NORMO NORMO. → TEAR drop cells. b) ↑ WBCs → IMMATURE LEUCOCYTOSIS. 2) BM BIOPSY ⇒ dry tap from ASIS (hairy cell leukemia / Myelo-fibrosis)		1) BLOOD: • ↑↑↑ ESR > 100. • Electroph. ⇒ MONOCLONAL Ig. (if NORMAL..) • ALP ⇒ NORMAL (No ⊕ of OSTEO-blasts) • β₂ Microglobulin → for follow up. 2) URINE ⇒ +VE BENCE JONES PROTEINS (LIGHT CHAIN Ig). 3) BM (DIAGNOSTIC) ⇒ plasma cells > 20%		Electrophoresis ⇒ IgM
A ₁ ↑ Red cell mass.	B ₁ ↑ Platelet > 400.000													
A ₂ NORMAL O₂ (↓ EP) ^{no} exclude hypoxia in 2 nd polycyth.	B ₂ ↑ TLC > 12.000													
A ₃ Splenomegally	B ₃ ↑ ALP. (WBCs ARE MATURE)													
	B ₄ ↑ Vit. B ₁₂ (CML & PV)													

TREATMENT

<i>poly-cythemia Rubra-Vera</i>	<i>Myelo-fibrosis</i>	MULTIPLE MYELOMA	<i>Walden-strom's</i>
1) hydroxy UREA (CHLORAMBUCIL & RADIO-ACTIVE P → ACUTE LEUKEMIA) 2) Symptomatic: - hyper-URICEMIA ⇒ Allopurinol. - hyper-viscosity ⇒ Thrombolytic th. ↑ platelets ⇒ Aspirin - Itching ⇒ Anti-hist. + avoid hot baths. 3) VENESECTION ⇒ keep PCV < 45%.	1) hydroxy UREA 2) Symptomatic - FOLIC A., IRON. SPLENECTOMY IN HYPER-SPLENISM. - AIHA → STERIODS WITH. - BL. TRANSFUSION + BM. 3) BM TRANSPLANT.	SUPPORTIVE TTT. - hyper-CALCEMIA ⇒ Bisphosphanate. - INFECTIONS ⇒ PNEUMOCOCCAL v. + ABs. - hyper-VISCOSITY \$ ⇒ plasmapheresis. - IV γ globulin. SPECIFIC Melphalan. V A D. Thalidomide?! TERATOGENIC...phaco-malia.	<i>Plasmapheresis</i> <i>Cytotoxic drugs</i>



Iron ↓ Anemia

"M/C CAUSE OF ANEMIA IN THE WORLD"

- 1) ↓ **INTAKE:** infancy > 6M/ ANOREXIA /old AGE.
- 2) ↓ **Absorption:** ↓ HCl – ANTACIDS – PHYTATE (CEREALS)
- 3) ↑ **DEMAND:** PREGNANCY – Adol. growth spurt.
- 4) ↑ **Loss** ⇒ **Chronic blood loss in Adults + انظر الاطفال**
 - a) **GIT bleeding:**
 - PU. Ankylostoma.
 - EV
 - b) **UTERINE bleeding.**

MEGALO-BLASTIC ANEMIA

Vit. B₁₂

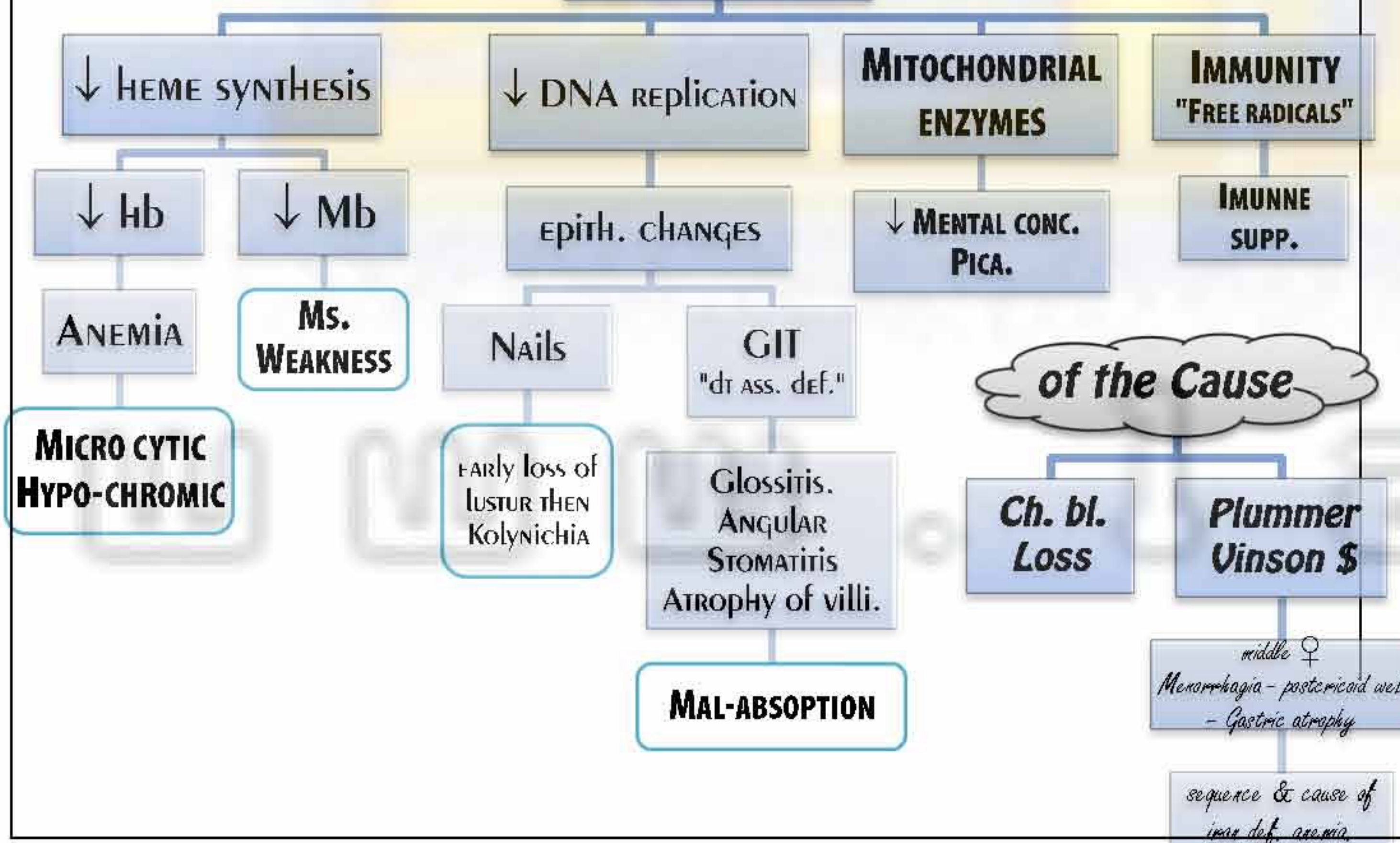
- 1) ↓ **INTAKE** STRICT VEGETARIANS "v. RARE dt ↑ STORES".
- 2) ↓ **Absorption from:** **الاسباب خطيرة لأن المخزون كبير**
 - a) **STOMACH** → dt ↓ **INTRINSIC F.**
 - **PERNICIOUS AN.**
 - **G. Atrophy.** (A = Auto-immune type)
 - **GASTRECTOMY.** (B = Helico-bacter)
 - b) **T. ileum:**
 - **MAL-ab. \$** tropical sprue / Crohn's D.
 - **B₁₂ Utilization** by bacteria + D. latum.
- 3) **DRUGS** Colchicine, NEOMYCIN ⇒ ↓ BM uptake of B₁₂.

Folic Acid

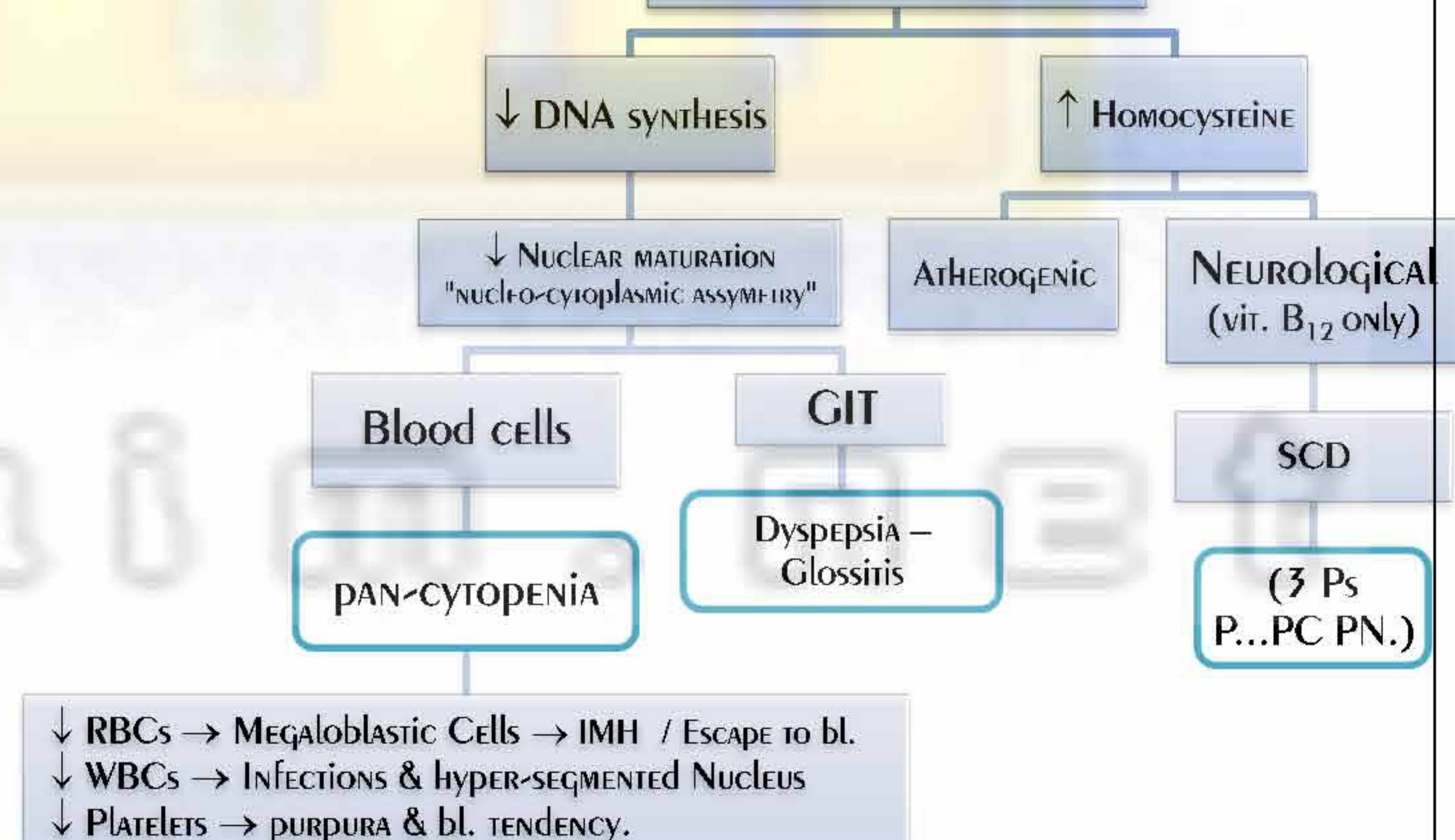
- 1) ↓ **intake** (IN ALCOHOLICS)
- 2) ↓ **absorption** Malab. \$.
- 3) ↑ **Demand** **preg. hemolytic crisis**
- 4) **Drugs:** phenytoin – cytotoxic drugs, 6 MERCAPTOPYRINE.

➤ **Cl./P = G. features of anemia +**

Iron def.



B₁₂ & Folic Def.



Iron ↓ Anemia

MEGALO-BLASTIC ANEMIA

INVEST.

- **ANEMIA?!** ↓ HB + ↓ RETICS.

- **MICRO-CYTIC HYPO-CHROMIC ANEMIA?!**

a) **BLOOD INDICES** ↓ MCV - MCH - MCHC

b) **BL. FILM** ↑ **RDW** (AN-ISO + POIKILO-CYTOSIS IN ANY DEF. ANEMIA)

- **Iron def. ?!**

1) ↓ **retics** + ↑ **platelets** (if active bl. Loss)

2) **Iron profile:**

- ↓ **IRON.**
- ↑ **IBC.** ↑ **FEP**
- ↓ **TRANSFERRIN SAT.**
- ↓ **S. FERRETIN.** "not accurate bec it is a phase reactant"

- **ANEMIA?!** ↓ HB

- **MEGALO-BLASTIC ANEMIA?!**

a) **BLOOD INDICES** ↑ MCV - MCHC: N.

b) **BL. FILM** **MACRO-CYTOSIS** + **HOWELL JOLLY BODIES.** "NUCLEAR REMENANTS"

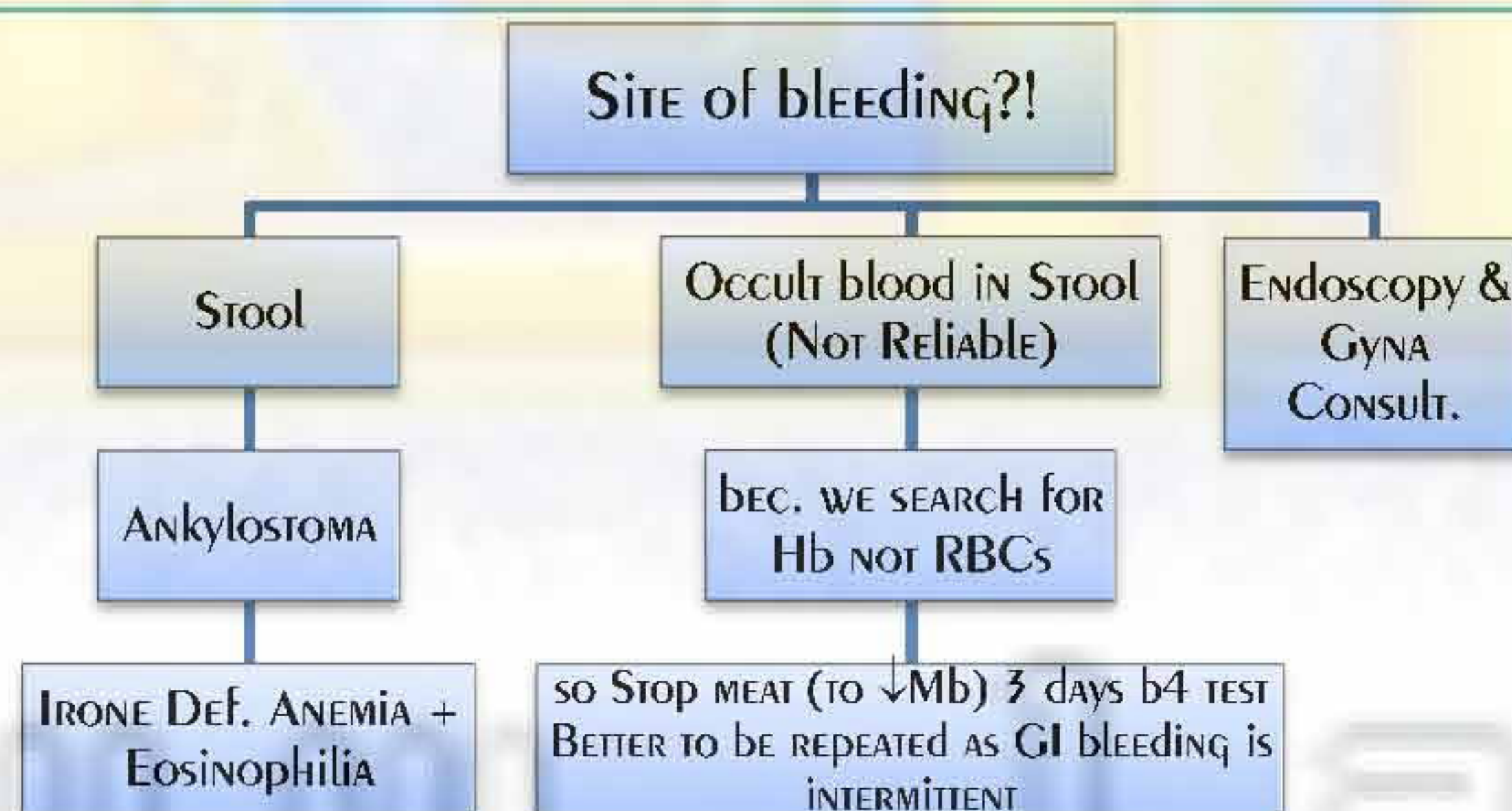
- **Vit B₁₂ def. ?!**

➤ **PAN-CYTOPENUIA:**

- a) ↓ **RBCs** dt → **IMH** → ↑ **S. bilirubin** + ↑ **LDH.**
- b) ↓ **WBCs** ⇒ **HYPER-SEGMENTED NEUTROPHIL.**
- c) ↓ **platelets.**

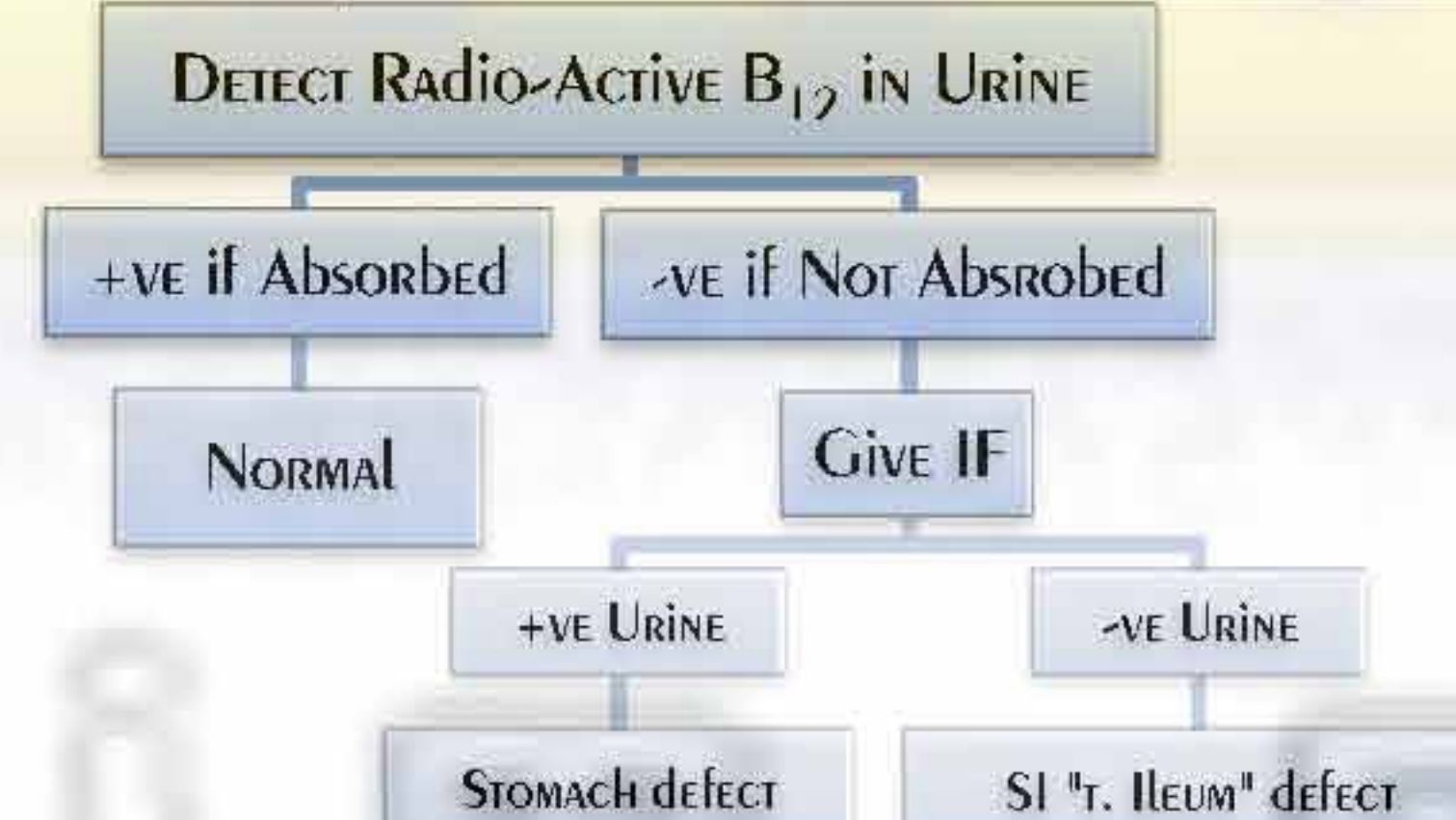
➤ ↓ **S. B₁₂** < 100

OF THE CAUSE?!



Anti-parietal & IF Abs +ve Schilling TEST to determine SITE of LESION

- **IM B₁₂ → SATURATE STORES → Oral Radioactive B₁₂.**



TREATMENT

Prophylactic

- 1) **ADEQUATE Fe FOR PREGNANT.**
- 2) **Fe SUPPLEMENTS AFTER THE 4TH MONTH** (EARLIER IN PRE-MATURE

CURATIVE

- 1) **IRON THERAPY.** (SEE LATER)
- 2) **BL. TRANSF.** (PACKED RBCs IF SEVER)
- 3) **of the CAUSE** EV - PU - ANKYLOSTOMA

Vit B₁₂ Hydroxy-cobalamine IM.
PARENTAL NOT Oral dt ↓ Abs.

Folic A. Oral → 5 mg/d till improvement
then low MD. (1 mg/d)

Sideroblastic ANEMIA

HEME SYNTHESIS DISORDER = Ineffective BM Erythropoiesis

- Failure of Fe incorporation into proto-porphyrin in Normo-blasts.
- dep. Of Fe granules in mitochondria of Normoblasts in BM.
- Ringed shaped Sidero-blasts in BM. **"DIAGNOSTIC"**

CAUSES:

- 1) HEREDITARY → X-LR. "dt Abnormal B₆ metabolism"
- 2) ACQUIRED → Alcohol – **INH** – lead → (-) proto-porph. Synthesis.

INVESTIGATIONS:

1) **ANEMIA?!** ↓ HB + ↓ RETICS.

2) **MICRO-CYTIC HYPO-CHROMIC AN.?!**

- BLOOD INDICES → ↓ MCV - MCH - MCHC
- BL. FILM → **PAPENHEIMER BODIES IN RBCs.** (Iron granules in RBCs)
→ **DIMORPHIC RBCs.** (hypochromic & Normochromic)

3) **Sideroblastic ?!**

- a) **IRON profiles** → No IRON def.
- b) **Hb electroph.** → No Th. MINOR.
- c) **BM EXAM. "DIAGNOSTIC"** → Sidero-blasts + ↑ IRON STORES.

TREATMENT: Stop the drug + Vit. B₆ "high dose"

PERNICIOUS ANEMIA

- B₁₂ def. → MEGALO-blastic ANEMIA.
- Dt AUTO-IMMUNE Abs against IF, parietal cells.
- ASSOCIATIONS: other autoimmune e.g. myxedema, thyroiditis, vitiligo – DM type 1.

**MICRO-CYTIC HYPO-CHROMIC AN.
BUT NOT RESPONDING TO TTT.**

	IRON def.	ANEMIA of CHRONIC D.	β THALASSEMIA MINOR	β THALASSEMIA MAJOR	Sideroblastic
RDW	↑	NORMO / NORMO	↑	↑	N
RETICS	N OR ↓		↑	↑	
IRON profile:					
• S. IRON	↓	↓	↑	↑	↑
• IBC	↑	↓	↓	N	N
• S. FERRITIN	↓	↑ OR N.	↑	↑	↑
• IRON STORES	↓	↑	↑	↑	↑ + Ring Sidero-blasts
Hb electroph.	N	N	↑ Hb A ₂ (α + δ)	↑ Hb F ↑ N ↓ Hb A ₂	N BL. FILM (PAPENHEIMER BODIES IN RBCs)

3 PARASITES & ANEMIA

- 1) ANKYLOSTOMA → IRON def. ANEMIA + Eosinophilia.
- 2) D. LATUM → Vit. B₁₂ → MEGALO-blastic AN.
- 3) MALARIA → HEMOLYTIC AN.

Iron Therapy

➤ **DOSE:** 3 – 6 mg / kg / d. **FOR 3 MNS TO fill THE STORES.**

➤ **ROUT:**

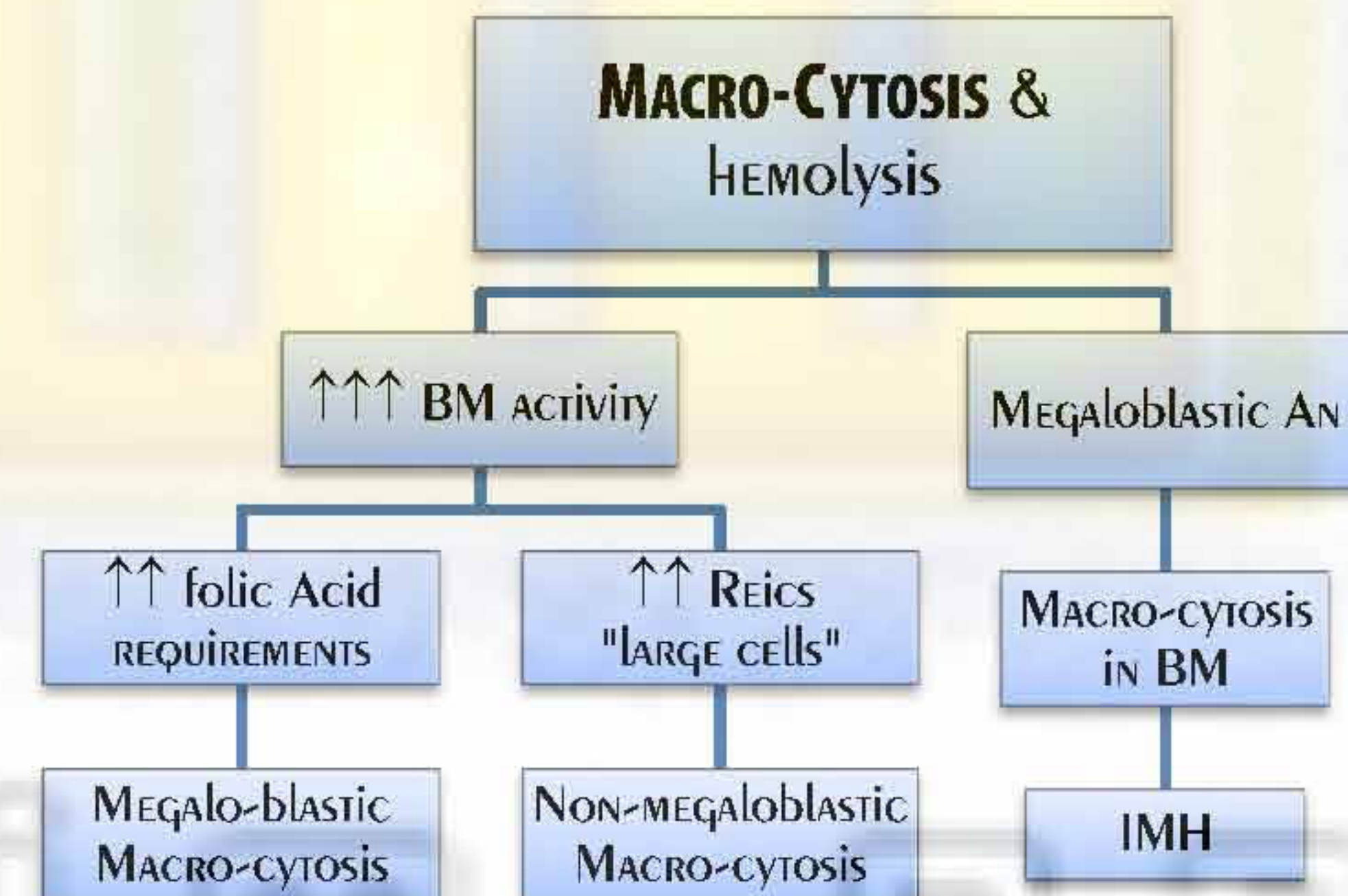
	ORAL	PARENTERAL
Type of IRON	• FERROUS SO₄ • FERROUS GLUCONATE. 3 divided doses bet. Meals & E Vit. C.	• IM → DEXTRAN. • IV → SACCARATED IRON (FROSAC)
	• ↑ Abs. → Vit. C. • ↓ Abs. → phytates - toxic A. & cereals.	INDICATIONS = FAILURE OF ORAL: 1) WRONG diag. "To Minor diagnosed as Iron def." 2) IRON INTOL. 3) MAL-Absorption \$. 4) Ch. HE. 5) Ch. INFECTION (IL₁ → ↓ BM utilization of Fe)
S/E	• GIT upset. (NV) • Constipation. "non-compliance" • Black stools. pt. should be informed	1) V. painful. 2) No control → toxicity.

➤ **RESPONSE TO TIT.:** ↑↑ NORMOBLASTS → Fe⁺⁺ → ↑↑ RETICS.

- 1st day → IMPROVEMENT of GC & Appetite.
- 2nd day → ↑↑ BM RETICS.
- 3rd day → ↑↑ periph. RETICS upto 5%.
- 4th day → GRADUAL STEADY ↑ of Hb % (1 gm / wk)
- REGAINING of s. FERRITIN.

MACRO-CYTOSIS

	MEGALO-BLASTIC	NON-MEGALOBlastic
• CAUSES.	↓ Vit. B ₁₂ OR Folic A.	1) CHRONIC LD. 2) Alcohol excess. 3) hypo-Thyroidism. 4) RETICS. "in hemolytic crisis"
• PATH.	↓ NUCLEAR MATURATION.	→ ↑ FREE Cholesterol → ↑ fat deposits on periphery of RBCs → ↑ size of RBCs.
• BM.	MEGALO-BLASTS in BM.	NORMAL BM.



HEMOLYTIC ANEMIAS

ANEMIA dt $\uparrow$ RATE of RBCs
destruction $\rightarrow$ $\downarrow$ THEIR LS.

General features of CHA:

- 1) pallor. (ANEMIA)
- 2) JAUNDICE. (HEMOLYTIC)
- 3) Th. FACIES. (CHRONIC)
- 4) HSM. Esp. in Th. MAJOR.

ANEMIA = Pallor

Tissue hypoxia

comp. mechanism

- 1) CNS $\rightarrow$ dizziness.
- 2) Ms. $\rightarrow$ fatigue.
- 3) FTT.
- 4) CVS $\rightarrow$ Anginal pain.

Jaundice

"lemon yellow"

Gall Stones "more e spherocytosis dt
 $\uparrow$ Hb compensated from hyper-active
BM $\rightarrow$ CBD $\rightarrow$ Obstr. Jaundice
olive green - dark urine, - clay stool

J

comp. mechanisms

"doesn't occur in hemolytic crisis"

CVS

ACUTE
"hypoxia...VD"

CHRONIC

$\uparrow$ HR

TACHYCARDIA &
palpitations

$\uparrow$ SV

F. AS/PS
HEMIC MURMUR

ACUTE

$\uparrow$ RETICS
NORMOBLASIS

CHRONIC

BM exp.

Th. FACIES

EMH

HSM

Marked in Th. Major
dt Abnormal BM
hematopoiesis.

RBCs

$\uparrow$ 2,3 BPG

$\downarrow$ Hb affinity
to O_2

shift of O_2
TO TISSUES.

HEMOLYSIS

IVH "AHC"

Hb EMIA

$\downarrow$ HAPTO-globin
 $\downarrow$ HEMOPEXIN

"if SEVER" Hb URIA
HEMOSIDRINURIA

s. pallor

AHC

dark urine s. Jaundice

$\pm$ loin pain.

$\pm$ ARF.

$\pm$ Anemic HF.

$\pm$ fever & rigors

1) LIVER $\rightarrow$ cirrhosis.

2) SPLEEN $\rightarrow$ splenomegaly.
Hyper-splenism.

3) HEART $\rightarrow$ cardio M. $\rightarrow$ Arrhythmia.

4) LUNG $\rightarrow$ infiltrates.

5) SKIN $\rightarrow$ Muddy complexion
(J. + pallor + $\uparrow$ melanin dep.)

6) SC $\rightarrow$ skin ulcers.

EVH "CHA"

$\uparrow$ Fe

spleen++ dt
RES hyperplasia

$\uparrow$ s. ferritin
 $\downarrow$ IBC
 $\uparrow$ t. ferritin

repeated bl.
transfusion

HEMO-SIDROSIS "THALASEMIA MAJOR"

7) WBCs $\rightarrow$ recurrent inf.

8) PN

9) ENDOCRINE

- PITUITARY $\rightarrow$ DI
- PTH $\rightarrow$ hypo-calcemia
- PANCREAS $\rightarrow$ DM.

$\uparrow$ INDIRECT
Bilirubin

$\uparrow$ D. Bilirubin in
bile SECRETION

$\uparrow$ STERICOBILLIN
IN STOOLS

DARK STOOL

$\uparrow$ UROBILINOGEN
IN URINE

NO CHANGE IN
URINE COLOUR.

Alcholoric
JAUNDICE

INVESTIGATIONS FOR ALL CASES OF CHA

1) **ANEMIA?!** (↓Hb)

2) **HEMOLYTIC?!**

- RBC DESTRUCTION** → ↑ **INDIRECT bilirubin.**
- BM⁺⁺** → ↑ **RETICS / PLATELETS / TLC** (diff. from infection by ↓ Hb)
- BL. INDICES:** → **NORMO / NORMOEXCEPT**
 - MICRO / HYPO.** → **Th. MAJOR.**
 - MACRO-CYTOSIS DT:**
 - ↑ **RETICS.** (hemolysis – hqe – Response to IRON th.)
 - ↓ **Folic A.** in hemolytic crisis → **MEGALO-BLASTIC CRISIS.**
 - SPHERO-CYTOSIS** → **RELATIVE ↓ MCV → ↑ MCHC**
(SO BM EXAM ISN'T ESSENTIAL IN H. ANEMIA)
- IVH = (G6PD + AIHA "cold")** → ↓ **hapto-globin & hemopexin** + ↑ **LDH.**

3) **SPECIFIC?!** (BL. FILM + SPECIFIC TESTS)

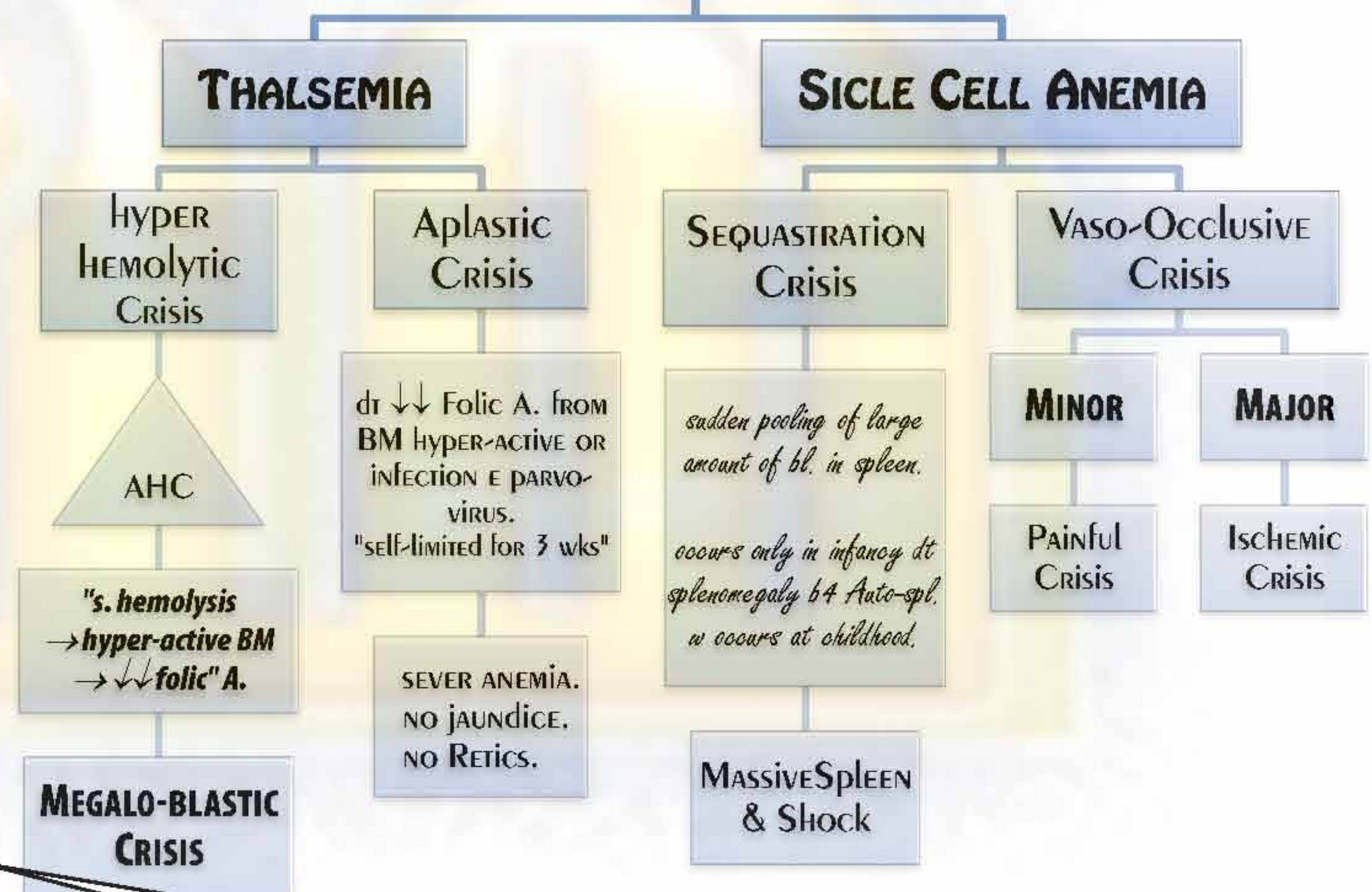
4) **X-RAY of CHA:**

- Skull** → **HAIR ON END APP. / WIDE DIPLOID SPACE.**
- LONG BONES** → **THIN CORTEX / WIDE MEDULLARY CAVITY / MOSAIC APP.**
- BONE DESTRUCTION** in **SCA.**

➤ **NB:**

- RBCs & labeled CHROMIUM** → **SPHERO-CYTOSIS & hyper-splensim.**
- ↑ **ESR** in **ANEMIAS EXCEPT (SPHEROCYTOSIS & SCA dt ↓ ROULEUX)**

HEMOLYTIC ANEMIA CRISIS



HEMOLYTIC AN. with NO SPLENOMEGALY:

- SCA** (splenomegaly in SCA = Sickl β-Thalasemia = $hbF + hbS$)
- G6PD**
- PNH.** (C3 comp.)
- AIHA.** (cold IgM Ab → IVH)
- Mech. hemolysis.**

THALASEMIA

↓↓ α CHAINS

α THALASEMIA

4 GENES ON α CHAINS
ON CHROMOSOME 6

↓↓ β CHAINS

HOMO-ZYGOUS

HETERO-ZYGOUS

$\beta^0\beta^0$

$\beta^+\beta^+$

$\beta\beta^+ / \beta\beta^0$

β-Th. MAJOR

β-Th. INTERMEDIA

β-Th. MINOR
"TRAIT"

DISCUSSED IN
DETAILS

MODERATE JAUNDICE &
SPLENOMEGALY.
(bet Th. MAJOR & MINOR)

DD (SEE BELOW)

CL./P of β -Th. MINOR:

- Mild anemia (micro / hypo)
- Splenomegally.
- Hb F & Hb A2 mildly ↑
→ mild symptoms.
- TTT.: family counselling.

	DEGREE OF ANEMIA	Hb electroph.
↓ 1 GENE	→ SILENT CARRIER. (TRAIT)	NORMAL
↓ 2 GENES	→ MILD ANEMIA.	NORMAL
↓ 3 GENES	→ MOD. TO SEVER. (MAJOR)	Hb H (β4)
↓ 4 GENES	→ "hydrops fetalis "incompatible e life"	Hb BART'S (γ4)

CAUSES OF PAN-CYTOPENIA IN β-THALASEMIA

	hyper-splenism	Aplastic An.	Folic A.
• ONSET	➤ GRADUAL.	➤ ACUTE ONSET.	GRADUAL dr ↑ Folic A. require by hyper-active BM. (6-8x)
• COURSE	➤ PROGRESSIVE.	➤ SELF-LIMITED.	
• DIAGNOSIS	1) PANCYTOPENIA + ↑ RETICS. 2) ↑ BL. TRANSF. 3) Radio-labeled RBCs Trapped in Spleen.	PANCYTOPENIA. + ↓ RETICS.	MEGALO-BLASTIC CRISIS.

CL./P

- 1) Mild hemolysis → mild ANEMIA.
- 2) **JUST palpable Spleen++** For DD. (Osis)

TTT. No need for TTT. but Family Counseling.

INVEST. MICRO-CYTIC HYPO-CHROMIC ANEMIA (SEE BEFORE)

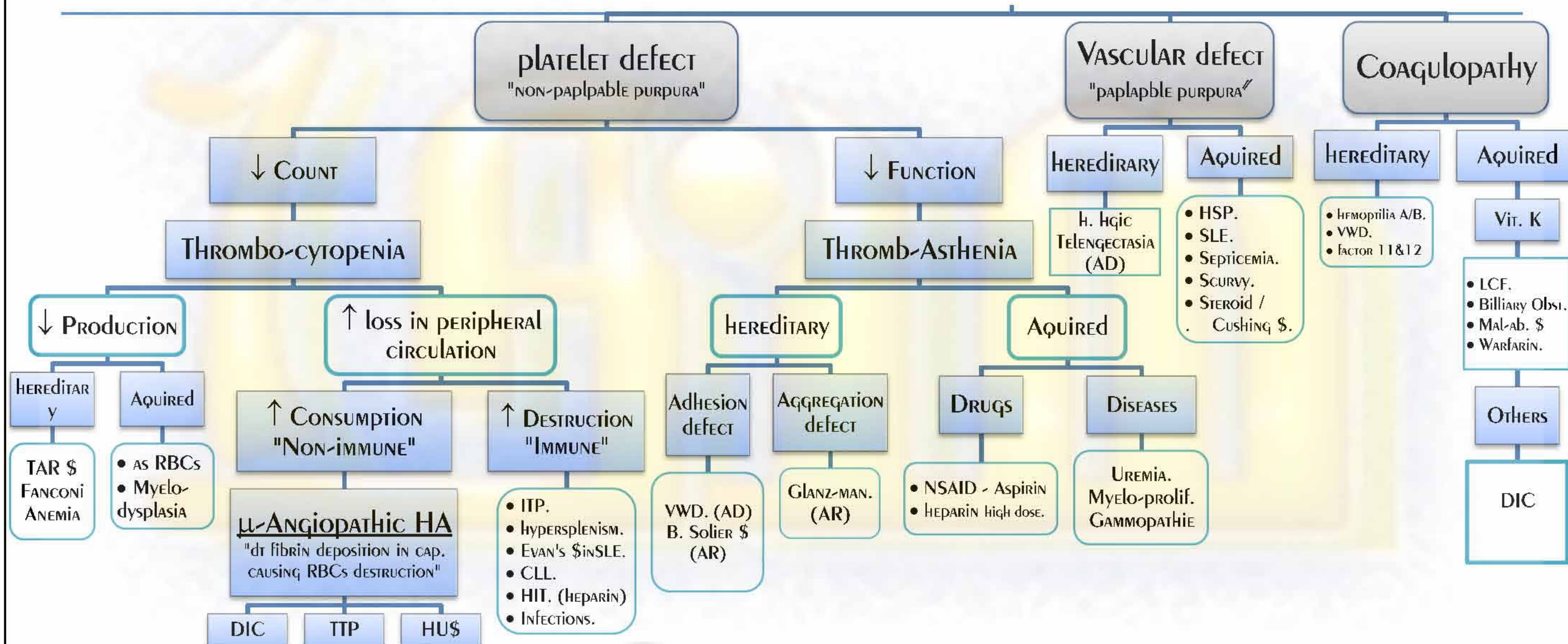
H. SPHEROCYTOSIS	β-THALASEMIA MAJOR	Sickle Cell ANEMIA (SCA)	G6PD DEF.
AD (NO FH IN 10-20%)	AR ⇒ ↑Hb F (70 - 80%)	AR (INTERMEDIATE INHERIT. / Co-dominant / INCOMPLETE AD)	X-LR
Hereditary CM defect ↓ spectrin "↓ membrane phospho-lipid" Integrity of CM Deformed RBC ↑ Na & H₂O permeability Spherocyte Rigid CM... Trapped in Spleen ⊕ Na/K ATPase ... "↓ ENERGY STORES" Osmotic fragility TEST EVH ↓ LS of RBCs Auto-hemolysis at 24 - 48 hrs "corrected b adding G."	<i>inability to form β-chain</i> ↑↑↑ α chains ↓ β chains ↑ γ chains IMH OF RBC PRECURSORS MEMBRANE DEFECT INEFFECTIVE BM ERYTHROPOIESIS RBCs CAN'T PASS RES ⊕ EMH EVH RES ++ HSM + Repeated bl. Trans. → ↑Fe load HEMOSIDROSIS μ cytic hypo-chromic an. (dt Incomplete switch off) ↑ Hb F "high O₂ Affinity" T. hypoxia ↑ EP BM ++ Th. FACIES ⊕ EMH HSM	HbS de-oxygenation dt... (Hypoxia - Dehydration - Infection) → Insoluble Hb → polymerization → filaments (hb) → Sickling of RBCs Trapped in Spleen ↑ BL. viscosity EVH (Chronic) Vaso-occlusion (INTERMITTENT ATTACKS)	↓ G6PD (SOURCE OF NADPH IN HMP SHUNT) ↓ ↓ Reduced GLUTATHIONE ↓ RESIST TO OXIDATIVE STRESS (DRUGS - INFECTION - FAVISM) PROTEIN lipid peri-ox. Hb denat. DEST. of CM PPT. IN RBCs AS HEINZ BODIES IvH
➤ CL/P			
ONSET: NEO-NATAL JAUNDICE GENERAL as CHA but e 3 diff. 1) NEONATAL ONSET of hemolysis. 2) HUGE Spleen SINCE infancy. 3) ↑ Gallstones dt ↑ D. BILIRUBIN <i>"Although Thalassaemic hemolysis > Spherocytosis but No Gall stones in Th. bec. RBCs are hypo-chromic → small Hb released during hemolysis"</i>	ONSET: AFTER 6 MS. (start of ↑β activity) GENERAL as CHA + COMPLICATIONS... 3 HIB 1) HEMO-sidrosis. (dt REPEATED bl. TRANSF.) 2) HYPER-splenism. (PAN-CYTOPENIA + ↑ Retics) 3) INFECTIONS. (DUE TO 1 & 2) 4) hF dt (1 + s. ANEMIA + TOXIC myo) 5) of BL. TRANSFUSION.	ONSET: AFTER 6 M GENERAL as CHA + Ch. LEG ULCERS dt HEMOSIDROSIS & VASC. OCC. AUTO-splenectomy "dt repeated splenic infarcts" FUNCTIONAL hypo-splenism ↑ INFECTIONS "Staph. & Salmonella" & THROMBOSIS ACUTE CRISIS (ALL 4) VASC. OCC. MINOR MAJOR PAIN CRISIS "H & F \$" ISCHEMIC INFARCTS SEQUESTRATION sudden pooling of large amount of bl. in spleen, occurs only in infancy dt splenomegaly b4 Auto-spl. w occurs at childhood. MASSIVE Spleen & Shock.	ONSET: MS. 1) AHC. 2) history of PDF. NB: No Splenomegaly EXCEPT in CHRONIC CASES. (v. RARE)
➤ INVESTIGATIONS * SPECIFIC			
1) Blood film ⇒ SPHEROCYTES (also appears in ALHA dt WARH Ab) 2) Osmotic fragility TEST. (Start at 0.7 % Normal at 0.4 %) 3) AUTO-HEMOLYSIS AFTER 24-48 HRS. (corrected by adding G.)	1) Blood film ⇒ TARGET CELLS 2) Alk. DENAT. TEST. (Hb F is RESISTANT) 3) Hb ELECTROPHORESIS ⇒ ↑ Hb F. 4) ANTENATAL diag. by DNA ANALYSIS of CVB.	1) Blood film ⇒ Sickle cells. (If bl. is Oxyg. in AIR ..NO sickling) 2) Sickling TEST ⇒ blood + Na bisulphate → hypoxia → sickling. (or squeeze finger → ischemia) 3) Hb ELECTROPHORESIS ⇒ ↑ Hb S. 4) ANTENATAL diag.....	1) Blood film ⇒ HEINZ bodies 2) G6PD ASSAY TEST. Immediately AFTER li. Retic & young RBCs are rich in G6PD ↓ INACCURATE After 6-9 wks steady state ↓ ACCURATE

➤ TREATMENT OF HEMOLYTIC ANEMIAS

	H. SPHEROCYTOSIS	β-THALASEMIA MAJOR	Sickle Cell ANEMIA	G6PD DEF.											
1) BL. TRANSFUSION 2) IRON CHELATION 3) Folic A. 4) <u>SPLENECTOMY?!</u>	Clinical improv. only but RBCs REMAIN SPHEROCYTES. <u>INDICATIONS:</u> 1) Cass e Bl. Transfusion. 2) S. hemolysis. 3) One of the FM died.	<u>NOT CURATIVE but good</u> "bec. the main site of Hemolysis in Th. is BM (IMH) not Spleen → <u>so INDICATIONS of Spl.?!?</u> a) <u>hyper-splenism</u> (↑ Bl. Transf > 300 ml packed RBCs / kg / yr.) b) <u>HUGE spleen e mech. DISCOMFORT.</u> c) <u>TRAUMA & RUPTURE spleen</u> even if b4 5 yrs.	• <u>AUTO-splenectomy.</u> • <u>SEQUEST. CRISIS.</u> (if RECURRENT OR RESISTANT)	of NO VALUE.											
5) Specific TTT.?!?	<u>CHOLECYSTECTOMY AFTER SPLECENTOMY</u>(if gall STONES)	1) <u>BM TRANSPLANT. "of choice"</u> 2) <u>DRUGS ⊕ hb F TO</u> → ↑ γ activity. → ↓ unopposed α-chains. → ↓ hemolysis. 3) <u>GENETIC COUNSELING.</u>	1) <u>SEQUEST. CRISIS:</u> → whole bl. TRANSF. 2) <u>VASO-OCC. CRISES:</u> a) MINOR → Analgesic - O₂ - NaHCO₃ - fluids. b) MAJOR → Exchange transf. in life threatening conditions to replace HbS e HbA₁ (Acute Chest S) 3) <u>DRUGS ⊕ hb F</u> ⇒ ↓ sickling of hbS (hydroxy UREA OR BUTYRATES)	1) <u>Avoid (DRUGS – INFECTIONS – FAVISM)</u> 2) <u>Alk. DIURESIS</u> to avoid acid hematin deposition. 3) <u>BL. TRANSFUSION DURING THE ATTACK</u> avoid Anemic HF.											
Splenectomy?! ↓ Tuftsins ↓ Opsonization of ENCAPSULATED ORG. SO BEFORE spl. VACCINES pNEUMO-COCCAL MENINGIO-COCCAL H. INFLUENZA. AFTER spl. PENICILLIN V till 6ys If infection OCCURS → Hosp. + IV ABs ↓ platelet DEST. THROMBO-cytosis low dose Aspirin PYRUVATE KINASE DEF.: • AR TRAIT. • <u>CBC:</u> NORMO / NORMO. <u>NORMAL RBC morphology.</u>		Sickle Cell Trait • HETEROZYGOUS. (SA) • BLACK RACES resist p. falciparum. • ASYMPTOMATIC. • <u>Sickling only in s. hypoxia.</u> (CA OR high altitudes)	G6PD Types <table><tr><th></th><th>Type A</th><th>Type B</th></tr><tr><th>RACE</th><td>blacks</td><td>CUCASUANS</td></tr><tr><th>Deficiency</th><td>Mild</td><td>Marked</td></tr><tr><th>HEMOLYSIS</th><td>No EXCEPT in PDF.</td><td>MODERATE & ↑↑ e PDF.</td></tr></table>		Type A	Type B	RACE	blacks	CUCASUANS	Deficiency	Mild	Marked	HEMOLYSIS	No EXCEPT in PDF.	MODERATE & ↑↑ e PDF.
	Type A	Type B													
RACE	blacks	CUCASUANS													
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HEMOLYSIS	No EXCEPT in PDF.	MODERATE & ↑↑ e PDF.													

	AIHA dt WARM Ab	AIHA dt Cold Ab	PAROXYSMAL NOCTURNAL HB-URIA
DEF.	Ab ATTACKS RBCs AT 37 C in vitro. (M/C of hemolytic An. In Adult)	Ab ATTACKS RBCs AT < 37C in vitro.	Acquired defect in BM stem cell ⇒ Aplastic anemia.
etiology	<u>IgG ATTACK RBCs</u> ⇒ RBCs BECOME SPHEROCYTES . ⇒ ⊕ Splenic phagocyte Activity. ⇒ EVH in Spleen .	<u>IgM Ab ATTACK RBCs ⇒ IVH</u> (Paroxysmal Cold hb-uria <i>IgG Donath - landsteiner Ab dt 8 or Viral</i>)	<pre> graph TD A[As Sickle Cell Anemia (Hemolysis - Infections - Vasc. Occ.)] --> B[RBCs] A --> C[WBCs] A --> D[Platelets] B --> E[ABSENCE of GPI PROTEIN in CM] E --> F["⊕ C3 AGAINST RBCs DURING SLEEP (↓PH)"] F --> G[IVH (Hemolysis) SO NO Spleen++] C --> H[PNL dysfunction] H --> I[Infections] D --> J[AGGREGATION... THROMBUS.] J --> K[VASCULAR OCC.] K --> L[Budd - chiari \$] </pre>
Causes	<u>أسباب ساخنة</u> 1) 3L (lupus - leukemia (CLL) - lymphoma) 2) Viral - α methyl Dopa.	<u>أسباب باردة</u> • Viral. (IMN / EBV) ... NHL • Mycoplasma pneumonia. (problem)	
CL./P	• Hemolytic Anemia. • Of the Cause. • Just palpable spleen. (dt EVH)	• Hemolytic Anemia. • Of the Cause.	
INVEST.	1) of hemolytic AN. (↓Hb / ↑I. bilirubin / ↑Retics) 2) <u>Of the Cause = 3L</u> • lupus → ANA. • leukemia → BM EXAM. • lymphoma → LN biopsy. 3) <u>of AIHA</u> • +ve Coomb's TEST. (IgG ON RBCs) • Acquired Spherocytes. (dt attack of RBCs by IgG)	1) of hemolytic AN. 2) <u>of the Cause.</u> (viral markers of EBV) 3) <u>of AIHA → DIRECT COOMB'S TEST.</u> (IgM ON RBCs مسقعة) <pre> graph TD A[Spherocytosis] --> B[HERIDETARY] A --> C[AQUIRED] C --> D[AIHA (WARM = 3L)] </pre>	1) ↓ RBCs ⇒ recent flow cytometry. 2) ↓ WBCs ⇒ Leucopenia. 3) ↓ PLATELETS ⇒ Thrombocytopenia. 4) -ve Coomb's TEST. (C3 only with NO Ab) 5) +ve HAM'S TEST ⇒ Blood + Acid HEMATIN. (↓pH) ⇒ hemolysis.
TTT.	1) Of the Cause. 2) Steroid. 3) Splenectomy. (Acquired Spherocytosis) 4) Immuno-supp. (if NO response to Splenectomy)	1) Of the Cause. 2) Steroids. 3) Splenectomy is of NO value. (as it is IVH)	1) Steroids. 2) BM Transplant dt BM Aplasia. هذا المريض يتحول من Hemolytic An. To Aplastic An.

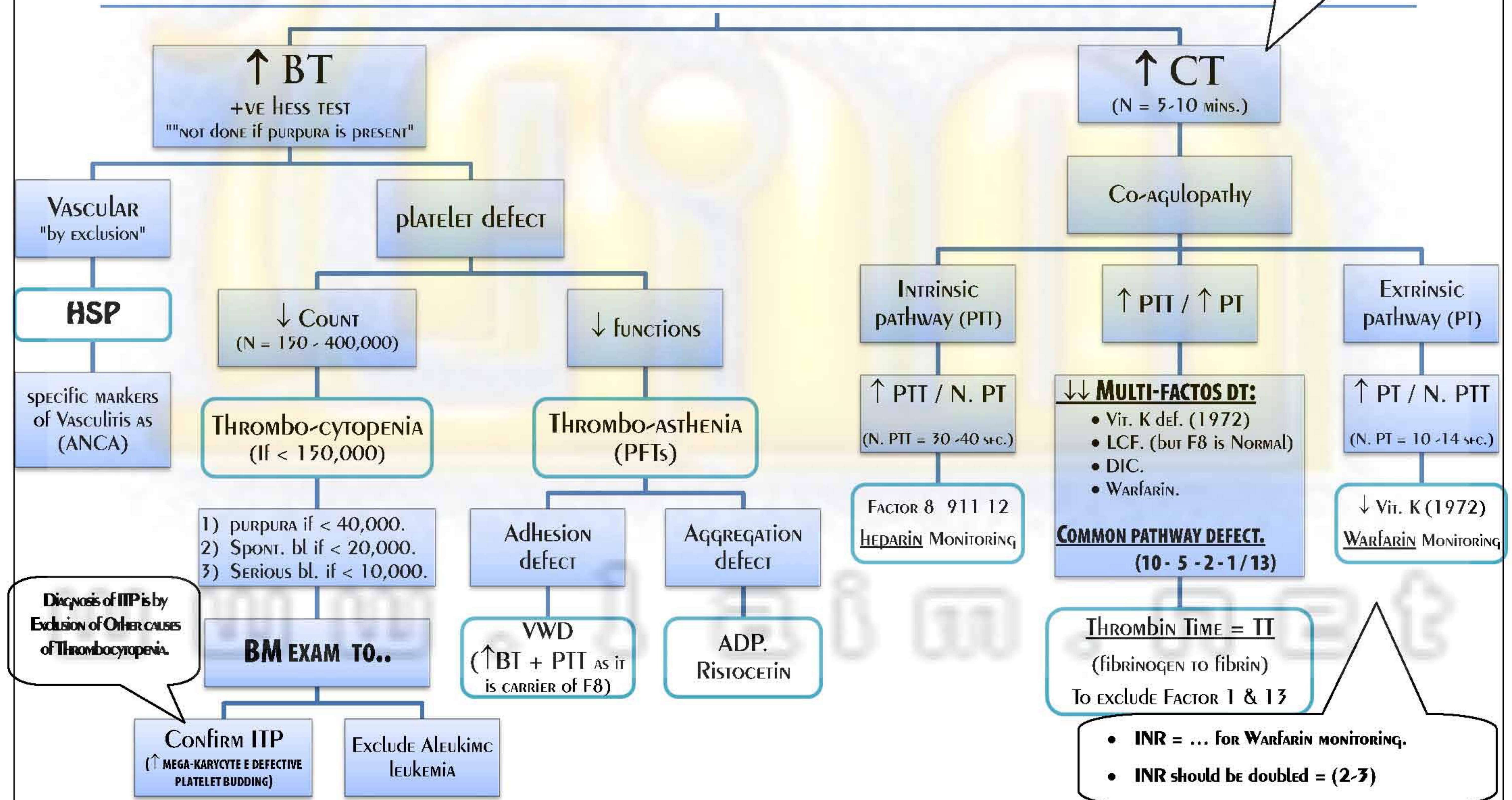
BLEEDING DISORDERS



TTP	HUS
Middle aged female	Child –postpartum
↓ RBCs → dt μ-ANGIOPATHIC HA.	
↓ platelets → Thrombo-cytopenia.	
جلطات في المخ و الكلى.	جلطات في الكلى فقط.

INVESTIGATIONS FOR BLEEDING TENDENCY

dt ⊕ of HEGMAN FACTOR W
TAKES A LONG TIME ... 4.5 MINS.



	purpura		coagulopathy																												
	Vascular defect = HSP	platelet defect = ITP	hemophilia A																												
DEF:	<u>HS III vasculitis (small vs.)</u> - post-strept-Viral or?! Drugs - Age → Children & young Adult.	<u>AUTO-IMMUNE DISEASE AGAINST platelets.</u> - Acute in Child → (post-viral) vaccines. - Chronic in Adult → Evan's S ⇒ AIHA + TTP	X-LR Deficiency of factor 8.																												
CL/P INVEST. (SCHEME)	1) ARTHRITIS: آه يا مفاصلي! - Big joint. - Non-destructive. - Migratory as Rh. fever. - Self-limiting. 2) Abd. Pain ⇒ mesenteric occ. آه يا بطني! 3) painless haematuria اده البول أحمر! - Nephrotic → FSGN. - Mixed → Mesangio-prolif. 4) palpable purpura on buttocks التوقع طفلي! 5) ± Allergy: itching / Wheals / Angio edema. NB: CNS stroke → focal lateralizing sign...neuro-exam.	Diagnosis is of ITP is by Exclusion of Other causes of Thrombocytopenia.	OTHER Complications - TRANSFUSION.... Hepatitis - AIDS → factor 8 - FORMATION of F8 Abs.																												
TREATMENT																															
	a) Self limited. b) STERIODS ⇒ for joint and abd. pains but do not alter the course.	<table border="1"> <thead> <tr> <th colspan="3">ACUTE ITP in Children</th> <th>Chronic ITP in Adults</th> </tr> <tr> <th>MILD</th> <th>MODERATE</th> <th>SEVER</th> <th></th> </tr> </thead> <tbody> <tr> <td><40,000</td> <td>20-40,000</td> <td><20,000</td> <td>STERIODS (↓ cap. Fragility / Ab / phagocytic activity of spleen)</td> </tr> <tr> <td>Asympt.</td> <td>Spont. BL</td> <td>Serious BL (ICH)</td> <td>↓</td> </tr> <tr> <td>Self-limiting</td> <td>Steroid القاعسة</td> <td> - IV Ig - Plasma conc. (To avoid Thrombotic Thrombocytopenia) </td> <td>SPLENECTOMY</td> </tr> <tr> <td></td> <td></td> <td></td> <td>↓</td> </tr> <tr> <td></td> <td></td> <td></td> <td>CYTOTOXIC D. & Block IgG.</td> </tr> </tbody> </table>	ACUTE ITP in Children			Chronic ITP in Adults	MILD	MODERATE	SEVER		<40,000	20-40,000	<20,000	STERIODS (↓ cap. Fragility / Ab / phagocytic activity of spleen)	Asympt.	Spont. BL	Serious BL (ICH)	↓	Self-limiting	Steroid القاعسة	- IV Ig - Plasma conc. (To avoid Thrombotic Thrombocytopenia)	SPLENECTOMY				↓				CYTOTOXIC D. & Block IgG.	Avoid trauma & anti-platelet. 1) REPLACEMENT th.: infusion EVERY 8hrs = 1/2 life of F8 (FF Plasma (10-15 ml/kg/3hrs.) ↑ IV volun by 30% - Cryo-ppt. -Factor 8) 2) HEMO-ARTHRITIS → passive exercise to prevent j. stiffness & fibrosis. 3) MM hqe → Anti-fibrinolytic. 4) DESMO-PRESSIN ⇒ ↑ level of factor 8 "mild cases"
ACUTE ITP in Children			Chronic ITP in Adults																												
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			↓																												
			CYTOTOXIC D. & Block IgG.																												

	HSP	ITP	HEMOPHILIA
INVEST.	Non-specific ○ ↑ IgA. ○ Complement..NORMAL.	a) ↓ platelet Count. b) B.M ⇒ hyperplasia of megakaryocytes. c) Ig G AGAINST plat. (NOT ESS. EXCLUSION OF OTHER CAUSES OF THROMBO-CYTOPENIA IS ENOUGH)	1) ↑ CT & N. BT. 2) ↑ PTT - NORMAL PT & plat. Count 3) ↓ factor 8. NB: 1) ↓ Factor 9 = (hemophilia B) SAME AS factor 8 . 2) ↓ Factor 12 = HEGMAN factor → ↑↑ PTT BUT NO bl. tendency.

VON Willebrand's D.	
Def.	(AD) Adhesion defect.
CL./P	PURPURA (platelet & Factor 8 dysf.)
INVEST.	SEE
TTT.	1) Factor 8 2) FFP / Cryo-ppt. 3) ADH (DDAVP) → RELEASE VWF

EVALUATION OF A CASE WITH BLEEDING TENDENCY

	Coag. Defect	Plat. Defect	Vascular defect
Type	Inherited	Acquired	Acquired
Sex.	MALE	FEMALE	FEMALE
F.H.	✓	×	×
CL./P	• HAEMATOMA. • HAEMOARTHROSIS • ECHYMOSIS.	• MUCOSAL (epistaxis) • PETICHAE WITHOUT RAISED EDGE	• PETICHAE with RAISED EDGE
compression	POOR effect	Good effect	Good effect
Bleeding	post- TRAUMATIC	SPONTANEOUS	TRAUMATIC

Hyper-coagulable State "Thrombo-philia"

HEREDITARY

Deficiency of Anti-Coagulants:

- 1) ↓ AT III. (dt heparin resistance)
- 2) ↓ **PROTEIN C** (dt warfarin th. without concomitant heparin)
- 3) ↓ **PROTEIN S.**
- 4) **FACTOR V LEIDEN** (Resist (-) by protein C)
(M/C inherited hypercoagulable state)

AQUIRED

- 1) **MALIGNANCY (Trousseau's S) Ch. DIC.**
- 2) **Behcet's D. (IVC Thrombosis)**
- 3) **Nephrotic S** (↓ AT-III – protein C, S)
- 4) **PREGNANCY & OCP** → ↑ **PROCOAGULANTS**
& ↓ **fibrinolytic** & (-) **PR.**
- 5) **Polycythaemia rubra vera**
- 6) **Essential Thrombocytosis.**
- 7) **Myelofibrosis**
- 8) **PNH.**
- 9) **Hyper-lipidemia.**

Anti-phospholipid S

RECURRENT THROMBOSIS Although ↑ PTT

RECURRENT THROMBOSIS in PLACENTA
→ **RECURRENT ABORTIONS.**

"DT Lupus Anti-coagulant & Anti-cardiolipin Ab"

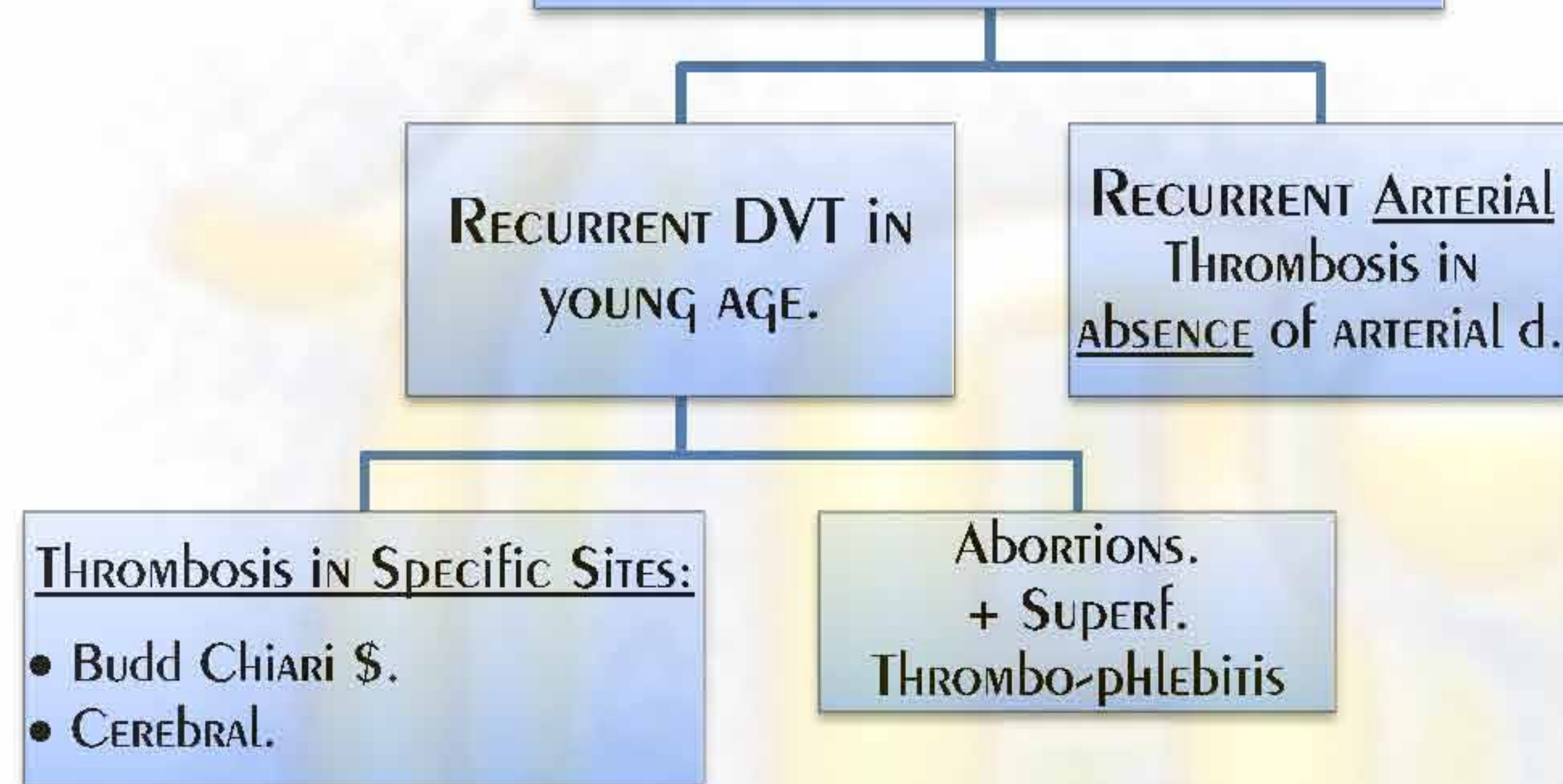
INVEST.:

- **Ab in vitro (test tube)** → ↑ **PTT** → **bl. tendency**
- **Ab in vivo** → **Thrombosis.**

TTT. ⇒ Warfarin.

- 1) **Steroids.** → (-) **Ab.**
- 2) **Anti-Coagulant & Anti-platelet.**
- 3) **Aspirin.**

Thrombophilia



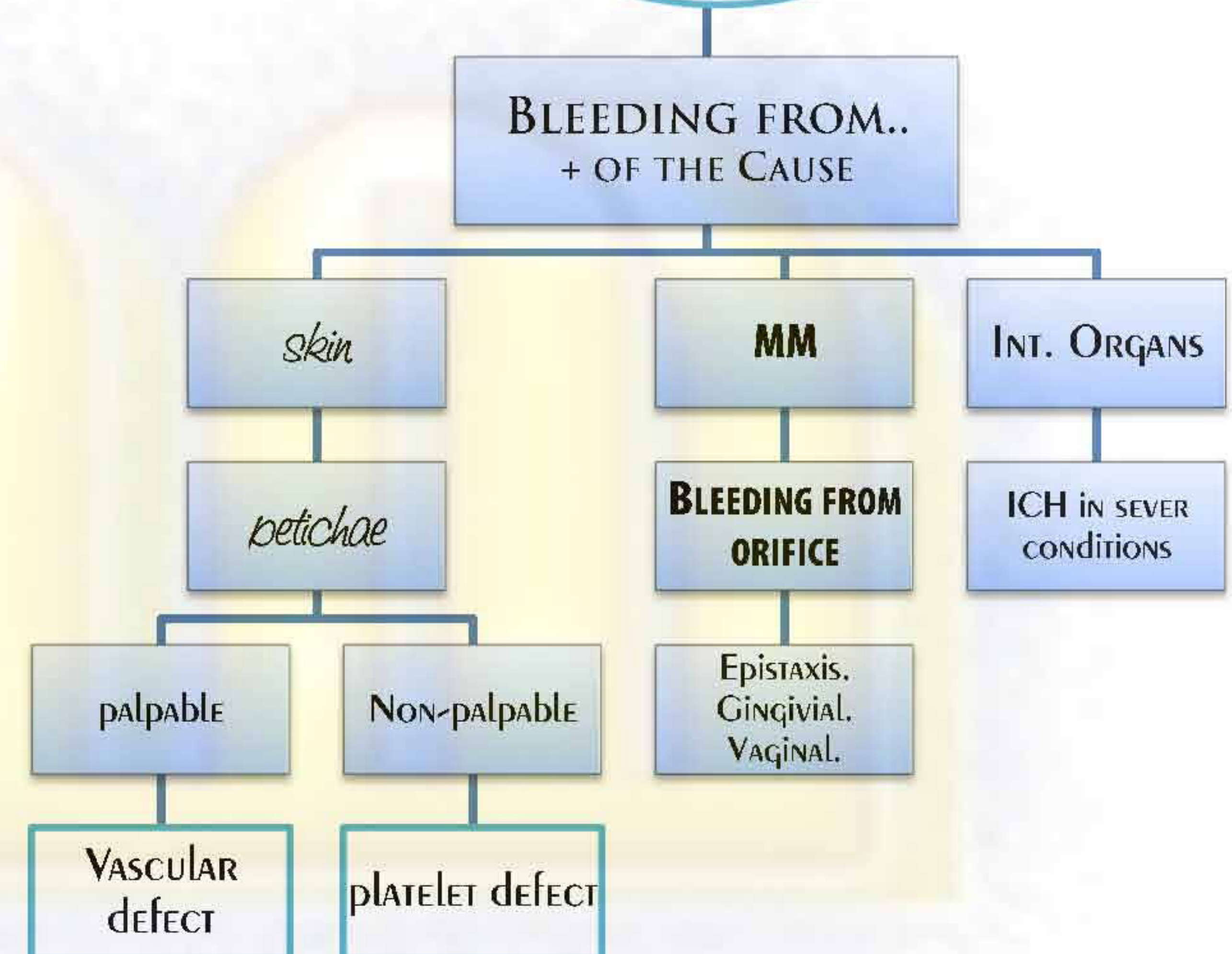
INVESTIGATIONS FOR THROMBOPHILIA:

- 1) $\uparrow\uparrow$ PTT.
- 2) HEREDITARY → THROMBOPHILIA GENE STUDY → $\uparrow\uparrow$ PROTEIN C, S AND AT-III FACTOR V LEIDEN.
- 3) Acquired:
 - CBC → Polycythemia + Thrombocytosis.
 - Nephrotic S. → UA.
 - Malignancies → TUMOR MARKERS, CT-SCAN.
- 4) Anti-phospho-lipid S → Lupus Anti-coagulants + Anti-cardio-lipin.
- 5) Duplex → site of thrombosis.

TREATMENT: قاعدة ذهبية

- a) CONG. DEFICIENCY → WARFARIN.
- b) MALIGNANCY → HEPARIN SC.

Cl./P of Purpura



DIC

TISSUE DESTRUCTION / ENDOTHELIAL DAMAGE

⊕ Clotting Cascade

Bradykinin Release

Fibrin deposition

Consumption of
Cl. factors & platelets

Arterial VD

Intra-Vascular Thrombi

Fibrinolysis

Hypotension

μ Angiopathic
Hemolytic Anemia

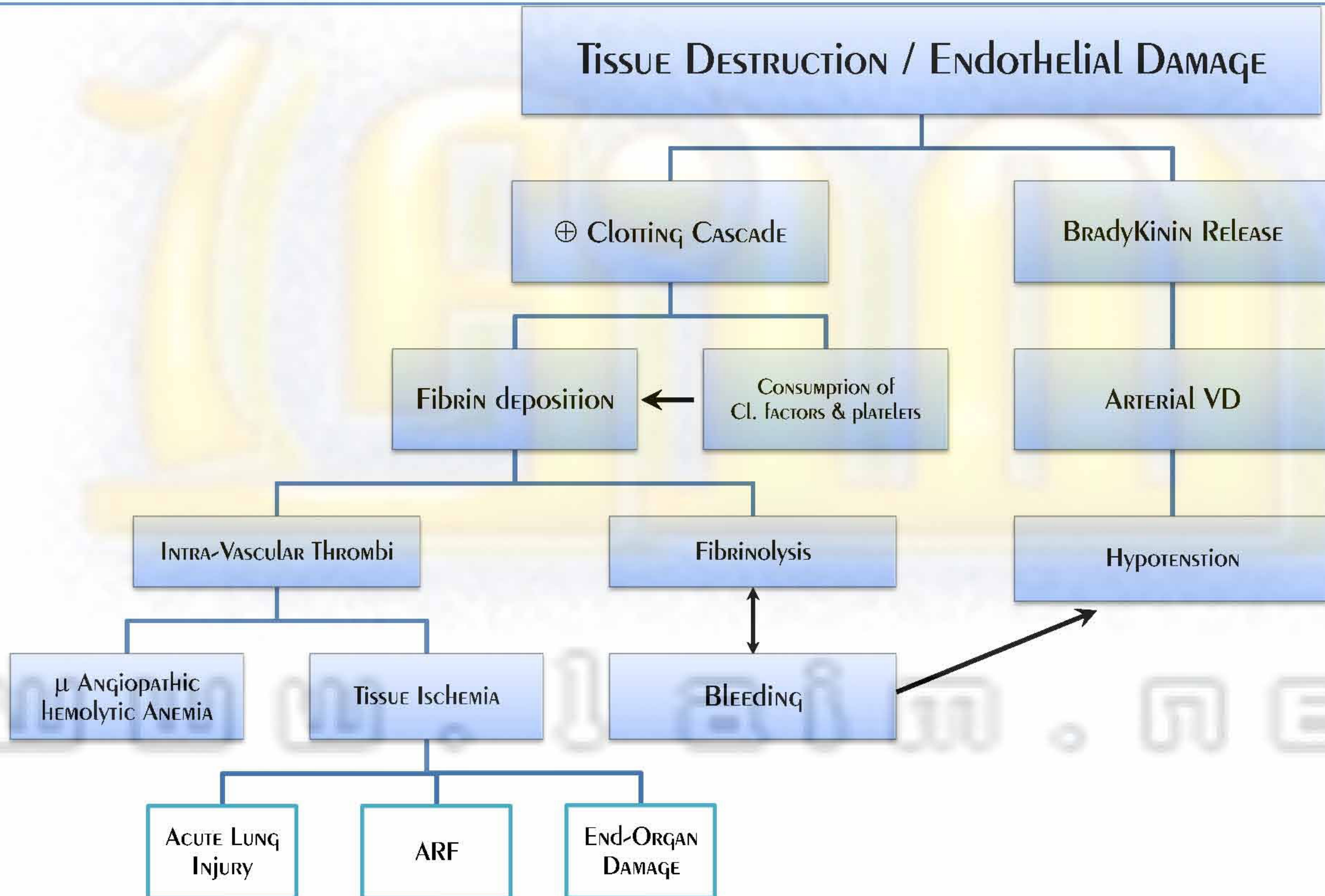
Tissue Ischemia

Bleeding

Acute Lung
Injury

ARF

End-Organ
Damage



DIC

consumption of coagulation factors due to $\oplus$ of intrinsic or extrinsic pathways $\Rightarrow$ fibrinolysis $\Rightarrow$ he or thrombosis

	Acute DIC	Chronic DIC
CAUSES	- Sepsis. - Amniotic Fluid - Abruptio placenta - AML = M₃ - ABO in compatibilities.	- Malig i.e. Trousseau's. - Retained dead fetus.
INVEST.	a) $\downarrow$ ALL ELEMENTS. $\downarrow$ Platelets. $\downarrow$ F 5 – 8 $\downarrow$ fibrinogen. b) $\uparrow$ ALL TIMES $\uparrow\uparrow$ PT - PTT $\uparrow\uparrow$ FDPs - $\uparrow$ D-Dimer. $\uparrow$ TT	$\downarrow$ platelet. (mild) - PT & PTT $\rightarrow$ Normal. $\uparrow$ FDPs. - Fibrinogen $\rightarrow$ Normal. - TT $\rightarrow$ Normal.

TTT. off DIC

- H_{qE} $\rightarrow$ FFP – fresh blood,
- $\downarrow$ platelets $\rightarrow$ platelet conc.
- Thrombosis $\rightarrow$ heparin.
- EA CA $\rightarrow$ AFTER heparin to avoid thrombosis.

	ACUTE HAEMOLYSIS	FEBRILE NON-HEMOLYTIC TRANSFUSION REACTIONS	DELAYED HEMOLYTIC TRANSFUSION R.
Def.	<u>occurs within minutes.</u> - Due to ABO incompatibility.	Due to anti-WBC or anti HLA Abs reaction with WBCs in the unit.	<u>occurs 5-7 days</u> after transfusion $\Rightarrow \oplus$ AB w was not detected at the initial cross match.
C/P	Acute: $\rightarrow$ Rigors and fever $\rightarrow$ Lumbar pain $\rightarrow$ Chest tightness $\rightarrow$ Hypotension	Fever – rigors – urticaria	Anaemia + J
ttt	- Stop transfusion. - Re- group & cross match again. - Check blood count, bilirubin - Monitor pulse, BP. - Support pt's circulatory state.	- Stop transfusion. - Exclude haemolytic reaction - Antipyretic - Use leucodepleted blood - Steroids if further bl. needed.	- Ab detection & spherocytes. - Compatible blood use.

Important Notes in BLOOD

p. 1 **Retics = hyper-active BM**

- ↓ in **Aplasia**.
- ↑ in (HEMOLYSIS – HE – IRON TH.)

p. 3 **ESR**

ESR

"Non-specific / used for follow up"

low

- 1) polycythemia rubra vera.
(Malignancy)
- 2) hypo-fibrinogenemia.
(DIC or partially clotted sample)
- 3) HEMOLYTIC ANEMIAS:
a) h. SPHEROCYTOSIS.
b) SCA.

mild or
Normal

PREGNANCY

Moderate

- 1) Infections.
- 2) ANEMIA EXCEPT...
- 3) MI (T. damage)
- 4) Inflammatory..
(SLE / RA)

v. high
> 100mm/hr.

- 1) **MALIGNANCY:**
 - LEUKEMIA.
 - LYMOHOMA.
 - Multiple Myeloma.
- 2) **CT disease.** (SLE / RA)
- 3) **Active TB - SEVER pyogenic.**

p. 4 **pt. E Hb 8 → MCV ... (ANEMIA مفتاح الـ)**

MCV

NORMAL

- 1) Aplastic.
- 2) HEMOLYTIC.

MACROCYTIC

- 1) MEGALO-blastic (Vit. B12)
- 2) NON-MEGALO-blastic.
(dt hyperlipidemia)

MICRO-cytic

- 1) IRON def.
- 2) THALASSEMIA.

p. 4

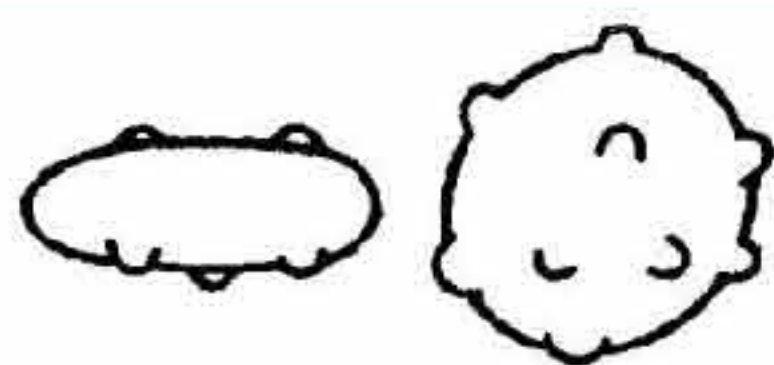
Abnormal Blood film (value of blood film)

• Microcytosis	IRON def. ANEMIA.
• MACROCYTOSIS	MEGALO OR NON-MEGALOBlastic AN.
• ANISOCYTOSIS = RDW (VARIATION IN SIZE)	MEGALOBlastic OR IRON def. AN.
• Poikilocytosis (VARIATION IN SHAPE)	Non specific.
• PUNCTUATE basophilia	lead poison.
• Howell Jolly bodies (SMALL ROUND NUCLEAR REMNANTS)	DysHAEMopoiesis = (MEGALOBlastic AN. & post-sPLENECTOMY)
• Pappenheimer bodies in	sideroblastic ANAEMIA.
• Polychromasia = ↑ Retics	HAEMOLYSIS.
• SHAPES of RBCs	(SEE LATER)

p. 5

Shape of RBCs in Different Diseases:

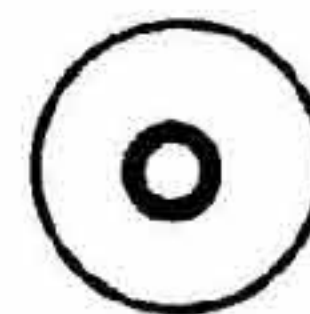
• BURR CELL	(ECHINOCYTE)	UREMIA.
• STOMATOCYTE	(MOUTH CELL)	HEREDITARY.
• TARGET CELL	(CODOCYTE)	THALASEMIA, IRON deficiency, LIVER D.
• ACANTHOCYTE	(SPUR CELL)	SPLENECTOMY, ADVANCED LD.
• SICKLE CELL	(LANCET CELL)	SCA.
• SPHEROCYTE		HEREDITARY, ACQUIRED (AIHA "WARM = 3L")
• ELLIPTOCYTE	(OVAL CELL)	HEREDITARY.
• SCHISTOCYTES	(HELMET CELL)	MECHANICAL HEMOLYSIS.
• TEAR drop cell	(DACROCYTE)	Myelofibrosis.



Echinocyte



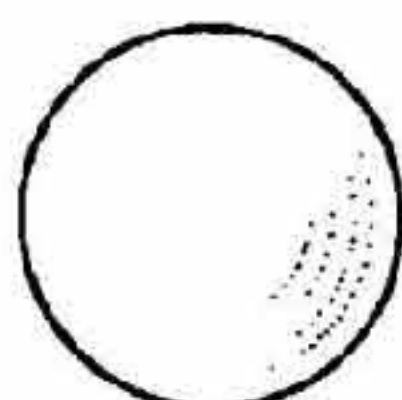
Stomatocyte



Codocyte



Acanthocyte



Spherocyte



Elliptocyte



Schizocyte



Dacrocyte



Sickle cell

p. 17

JAUNDICE in HEMOLYTIC ANEMIA:

- 1) **HEMOLYTIC CRISIS.**
- 2) **HEMPSIDEROSIS** → **IRON OVER-LOAD.**
- 3) **VIRAL HEPATITIS** → **dr bl. TRANSFUSION.** (↑AST / ALT)
- 4) **GALL STONE** → **CBD obst.** (↑ALP)

p. 29

JAUNDICE lymphoma**JAUNDICE in IMN**

- | | |
|--------------------------------|--|
| 1) AIHA. (WARM = 3L) | 1) AIHA. "Cold" |
| 2) LN in PORTA HEPATIS. | 2) VIRAL HEPATITIS. "↑TRANSMINASES" |

p. 26

ACUTE CHEST \$ in SCA:

Def.:	Specific Complication of SCA.
CL/P	Fever + hypoxia. (ARDS like)
INVEST.	1) ↑↑↑ leuco-cytosis. 2) CXR → lung infiltrates.
TTT.	Exchange Transfusion to ↓ HbS < 50%

p. 30

DRUGS CAUSING HAEMOLYSIS

- 1) Direct interaction with RBC membrane !? eg **Amphotericin.**
- 2) Immune mediated
 - a) **Methyldopa** → AIHA – Auto-immune hepatitis – Depression..
 - b) **Hapten type** → penicillins, cephalosporins.
 - c) **Innocent bystander** → Quinidine, Sulfa.
- 3) Drugs causing haemolysis in G6PD def. e.g. antimalarials, sulfa, nitrofurantoin.

p. 30

MECHANICAL HEMOLYSIS

- 1) **MARCH Hb URIA** → **HEMOLYSIS in FEET CAPILLARIES.**
- 2) **PROSTHETIC VALVE.**
- 3) **Calcific AS.**
- 4) **Microangiopathic HA** (fibrin deposition in capillaries → RBCs disruption)
(DIC - HUS - TTP - Malignant HTN, Scleroderma)

Diagnosis: Blood film → **schistocytes = helmet (fragmented RBCs).**

p. 30

TOXIC CAUSES of HAEMOLYSIS

- | | |
|------------------------|---------------------------|
| • Malaria. | • Staph. |
| • Clostridium welchii. | • Snake & Spider venom. |
| • Pneumococci. | Cu overload (Wilson's D.) |

Advanced LD → lipid abnormalities → spur-cell → haemolysis → Anemia.

p. 34

DD of pancytopenia.

- **Aplastic Anemia** → pan-cytopenia + No Retics.
- **hyper-splenism** → pan-cytopenia + ↑ Retics.
- **Folic Acid def.** → Megaloblasts in BM.

p. 40

Leukomoid Reaction = Leukemia like

- 1) **CAUSE: Infections (Abscess) – hemolysis – hge.**
- 2) **TLC <50,000/mm³.** → (Shift to the Lt.)
- 3) **↑ALP. Dt functioning WBCs. (in leukemia CML ...↓ALP)**
- 4) **CBC → Normal** → RBCs – Platelets – BM ... **No blasts.**
→ IMMATURE cells NEVER > 5%, but NEVER blasts.

p. 41

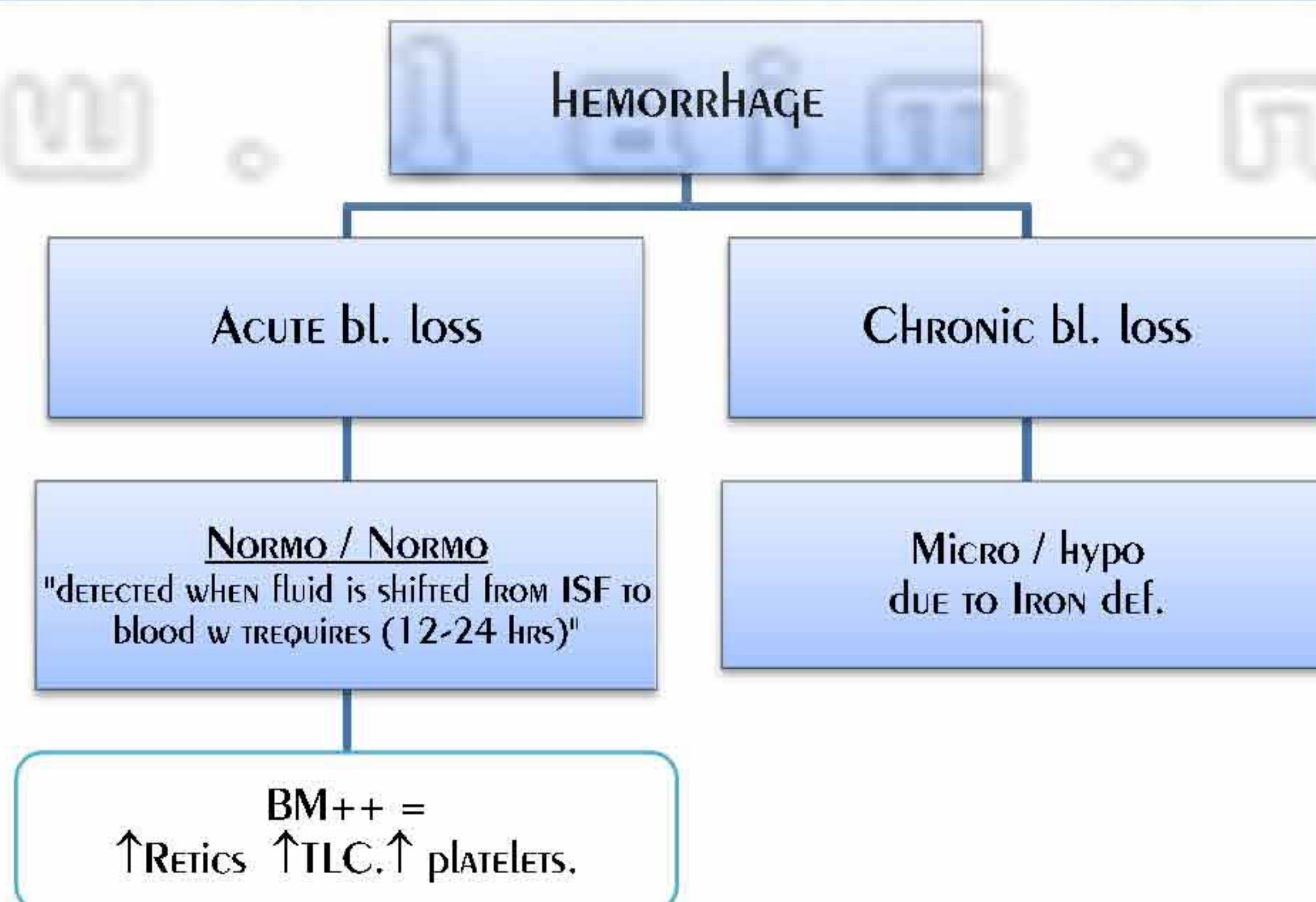
Leuko-Erythroblastic Reaction

IMMATURE BLASTS of WBCs / RBCs in peripheral bl.

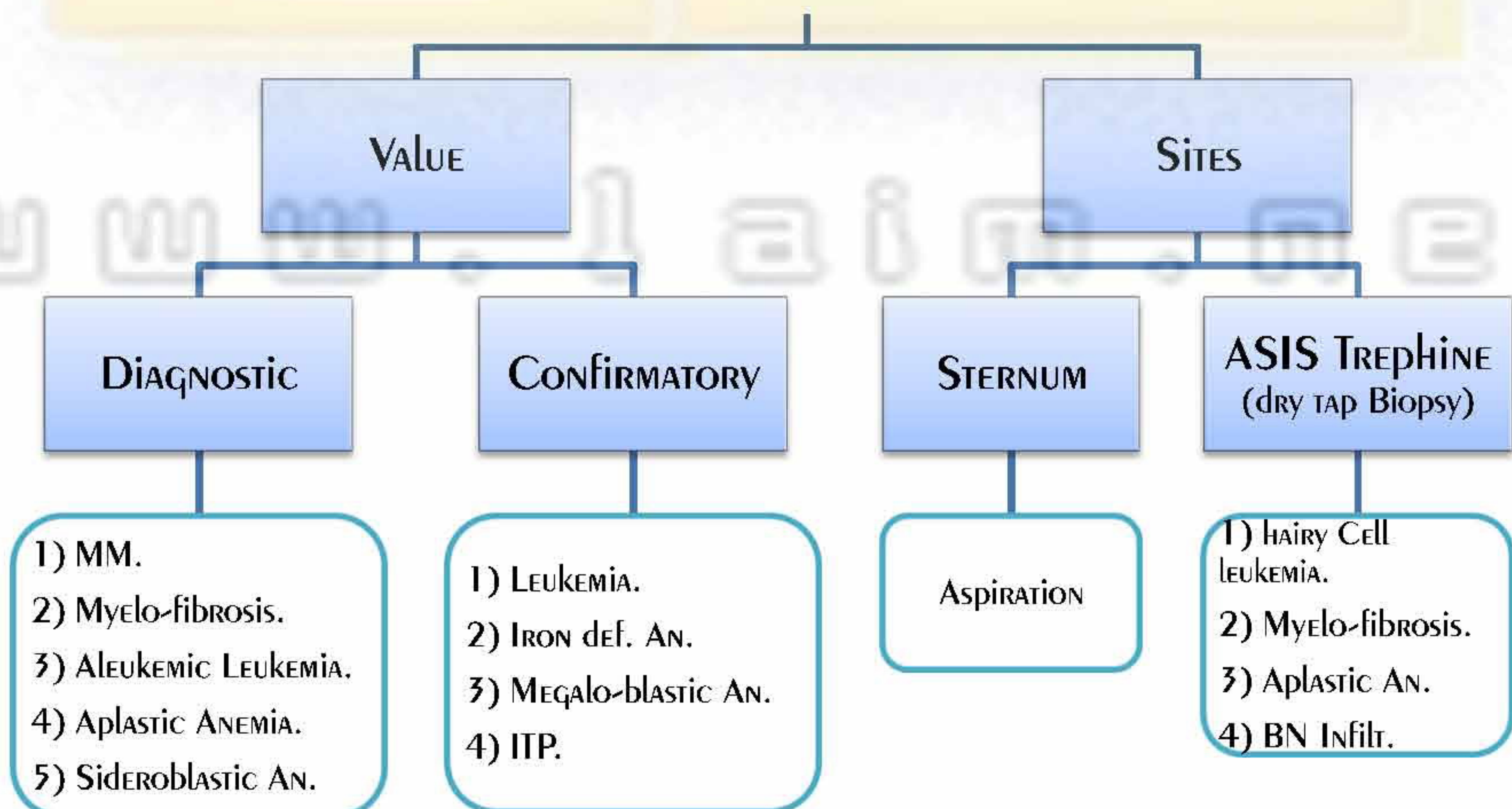
- 1) **BM infiltration:**
 - Leukemia.
 - Lymphoma.
 - Multiple Myeloma.
 - Myelo-fibrosis & TB.
- 2) **SEVER hemolysis – hge.**

p. 25

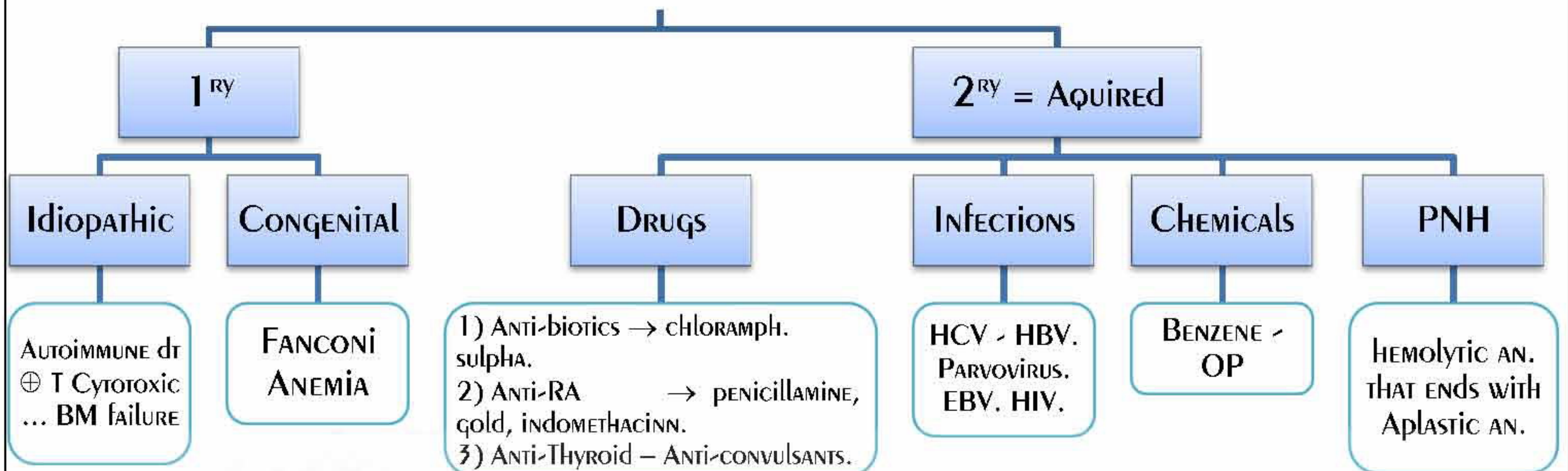
HEMORRHAGIC ANEMIA



	HYPER-SPLENISM	HYPO-SPLENISM
CAUSES	“↑ phagocytic Activity of Spleen → MONO upto PAN-cytopenia + BM[⊕]” <u>Splenomegaly due to any cause</u> 1) PH dt Cirrhosis. 2) CHA... 3) RA. (felty's \$) 4) Lymphoma, leukaemia, 5) Amyloidosis, Myelo-fibrosis.	1) Post-Splenectomy. 2) Auto- Splenectomy → SCA. 3) Congenital Absence.
<u>INVEST.</u>	1) Pan-cytopenia + ↑ Retics. (N. BM exam.) 2) RBCs e chromium in spleen.	1) Howell jolly bodies in RBCs, 2) Acanthocytes. (Chronic LD / post-splenectomy)
<u>Ttr.</u>	1) Transfusion 2) Splenectomy 3) ABS for infections.	• Vaccine for encapsulated org. (Pneumococcal & H influenza Meningitis) • Prophylactic penicillin.

BM EXAMINATION

Aplastic Anemia

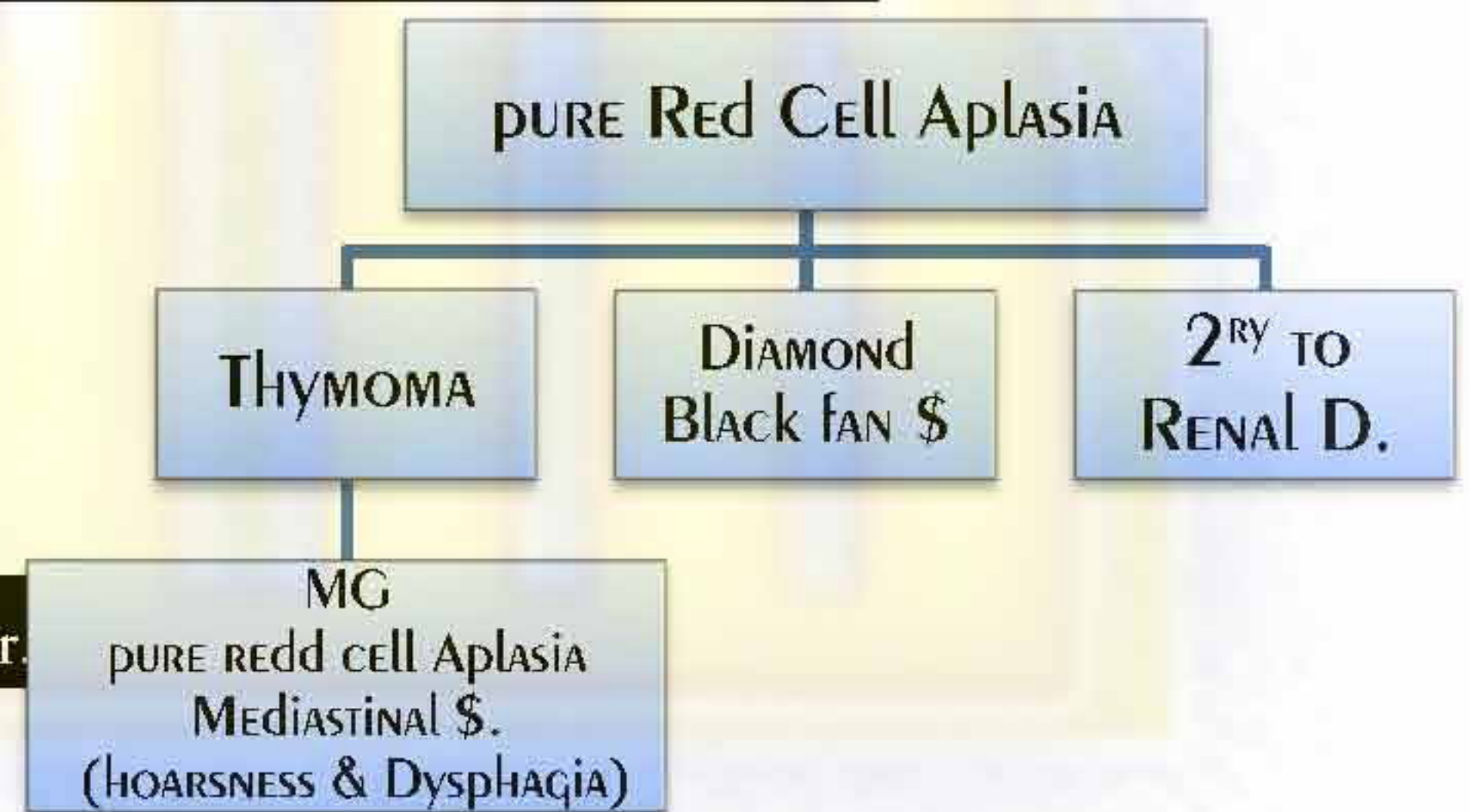


CL. /P = pan-cytopenia

- ↓ RBCs → **ANEMIA** → pallor.
- ↓ WBCs → **RECURRENT INFECTIONS** → (Sore throat + scanty pus)
- ↓ Platelets → **PURPURA**.

INVESTIGATIONS:

- **2^{ry} CAUSES MUST BE EXCLUDED.**
- **HISTORY of VIRAL INFECTION.**
- **CBC** → pancytopenia + No Retic.
- **BM EXAM.** → pancytopenia = hypo-cellular.



ANEMIA of CHRONIC DISEASE

CAUSES:

CHRONIC INFECTION → TB – Bronchiectasis.

CHRONIC INFLAM. → RA - IBD - Malignancy.

INVEST.:

- ↓ **RBCs** → **NORMO / NORMO. due to BM (-) by:**
 - ✓ **IL-1 & TNF** → Failure of iron utilization → ↑ Iron Stores +
↓ release from BM to Normoblasts → poor response to EP)
 - ✓ & Not by ...hemolysis – hge – BM infiltration.
- **NORMAL WBCS & PLATELETS.**
- **IRON profile** ⇒ ↓ s. IRON + ↑ IRON STORES. (↑ s. FERRITIN ..SEE ABOVE)

III.:

- 1) **OF THE CAUSE.**
- 2) **BM ⊕ by EP ⇒ POOR RESPONSE**
- 3) **NO RESPONSE TO IRON TH. dt failure of....**

LEUCOCYTES

	Neutrophilia	Eosinophilia	Basophilia	Monocytis
TLC Absolute	40-75% (2000-7000/mm³)	1-6% (20-500/mm³)	<2% (0-100/mm³)	2-9% (200-800/mm³)
CAUSES	- ACUTE pyogenic INFECTIONS. T. damage → burns, MI. - MALIGNANCY. - Myeloprolif. & Leukaemia (CML) - INFLAM. D. → RA. - DRUGS → CS. - ACUTE hge – hemolysis. - METABOLIC → UREMIA / Eclampsia.	- ALLERGY / DRUG HS. - PARASITIC → Hydatid - Fasciola - Ankyl. - ADDISON'S D. - Hodgkin's D. / Myelo-prolif. - VASCULITIS. (Churg-Strauss – Wegner's ± PAN) 1^{ry} hyperEosinophilic \$ + <u>INVASIVE TOXIC EFFECTS TO THE HEART AND LUNG.</u>	- Myelo-prolif. - IBD. - ACUTE HS. - REACTIVE. (Myxedema / Xanthemata)	1) <u>Bacterial</u>: TB – Brucellosis - S.A.B.E. 2) <u>Viral</u>: CMV, IMN. 3) <u>Protozoa</u>: (malaria). 4) AML. (M₄ - M₅) / CML 5) IBD

Lymphocytes

- TLC** = 20 - 40%.
- Absolute Count** = 1500- 3500/mm³.

Lymphocytosis	Atypical lymphocytosis	Lymphopenia	LIVER Spleen LN++ PERISTANT Lymphocytosis CLL "Old Age" Atypical Lymphocytosis CMV OR IMN "YOUNG AGE & SORE THROAT"	
<u>Viral</u>: IMN – CMV. <u>Bacterial</u>: TB - Brucella, Typhoid <u>Protozoal</u>: toxoplasmosis. <u>Malignancy</u> = Lymphoma, CLL.	<u>Viral</u>: IMN / CMV. - Lymphoma, leukaemia. - hepatitis.	- CS therapy. - Congenital Immunodef. - Chemotherapy. - HIV. – Hodgkin's.		

NEUTROPENIA (> 2000)

AGRANULOCYTOSIS (> 500)

1) INFECTIONS:

- **BACTERIAL** → TB – BRUCELLA – Typhoid
(if intestinal perf. ... peritonitis → leucocytosis).
- **VIRAL**: → HIV / hepatitis / INFLUENZA.

2) PAN-CYTOPENIA: APLASTIC AN. + hyper-splenism.

3) IMMUNOLOGICAL: SLE / Felty's \$ in RA

4) DRUGS:

- Anti-Inflam. / Anti-Bact.
- Anti-Convulsants / Anti-Cancer.
- Anti-thyroid / Anti-Diabetic.

➤ **INVEST.** NEUTROPENIA +
NORMAL RBCs & platelets.

➤ TTT.:

- 4) OF THE CAUSE.
- 5) G-CSF.
- 6) BM TRANSPLANT.

